BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019570
Article Type:	Research
Date Submitted by the Author:	14-Sep-2017
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Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

Does endometriosis affect professional life? – a retrospective matched case-control study

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Short title: Professional life in endometriosis

Word count: 3649

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Abstract

Objectives: Endometriosis is a gynaecologic disease causing severe and chronic pelvic pain as well as an impaired quality of life. The aim of this study was to investigate if and how endometriosis interferes with professional choices, career development and daily working life.

Design, setting and participants: Within a multicentre retrospective case-control study, we collected data from 505 women with surgically/ histologically confirmed diagnosis of endometriosis and 505 matched controls. Study participants were recruited in hospitals and private practices in Switzerland, Germany and Austria. The study investigated work life and career paths of participants using a detailed questionnaire.

Main outcome measures: Quantitative and qualitative parameters of professional life as well as associations between endometriosis related symptoms and loss of working power.

Results: Among women with endometriosis, chronic pain significantly increased sick leave (OR = 3.52, 95%-CI: 2.02 - 6.13, R^2 = 0.072, p < 0.001). Higher frequency of fatigue likewise related to increased sick leave (OR = 3.50, 95%-CI = 1.76 - 6.94, R^2 = 0.073, p < 0.001). Women with endometriosis had to consider health related aspects in their career decisions to a significantly higher degree than women from the control group (OR = 3.08, 95%-CI: 2.14 - 4.42, R^2 = 0.062, p < 0.001). However, most other direct associations between endometriosis and work outcomes were very weak (i.e., R^2 < 0.03). Notably, women with endometriosis did not experience higher stress levels at work than controls when adjusted for confounders (OR = 1.17, 95%-CI: 0.91 - 1.50, R^2 = 0.014, p = 0.211).

Conclusions: Endometriosis has a negative impact on professional life. Disease symptoms result in health-related limitations of career choices. Further research to develop strategies to support endometriosis affected women in realizing professional opportunities is recommended.

Strength and limitations of this study

This study presents one of the largest samples investigating the association between endometriosis and professional activity.

Recruitment of study participants in university, in district hospitals and in private offices supports a representative sample.

Validation of diagnosis and stage of endometriosis by operation reports provides high data quality.

A combination of objective data and the personal experience of women diagnosed with endometriosis provides valuable insight in professional activity on the background of the disease.

Given the retrospective design with a self-reported questionnaire, distortions in the sense of falsely or overly attributing professional dissatisfaction to endometriosis cannot be excluded.

Trial registration number:

Clin.trial.gov: Endo_QOL NCT02511626

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest

The authors do not have any conflicts of interest.

Data sharing statement

The data set is available on request from the corresponding author.

Key words: Endometriosis, work, professional life, stress, career choice

Introduction

Endometriosis is a gynaecologic disease, which is defined by the presence of endometrium-like tissue outside the uterine cavity.[1] The prevalence of the disease among women of reproductive age is estimated to be between 8 and 10%.[2,3]

Women suffering from endometriosis most commonly experience one or a multitude of the following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia, pain during defecation/ urination, loin pain, irregular bleeding, constipation/ diarrhoea, but also reduced fertility and chronic fatigue.[4,5] Numerous and severe symptoms, the chronicity of the disease, side-effects of therapies as well as the diagnostic delay[6,7] significantly affect women's global quality of life including professional performance and place high demands on the treating physicians.[8,9,10] For most patients, available treatment options, such as analgesics, different hormonal therapies, and radical laparoscopy[1] are often not curative and associated with significant side effects.[8,11]

Consequently, disease symptoms, especially endometriosis-associated pain and fatigue, may disturb the development and realization of long-term goals such as a professional career[12] as well as meeting demands on the job. About 40% of women with endometriosis report an impaired career growth through endometriosis[9], and about 50% experience decreased work ability due to their chronic disease.[8,13]

The quality of working life is a major aspect in overall quality of life,[14] which in turn is the most important predictor of total cost of disease.[15] About 66% to 75% of total costs of endometriosis arise from loss of working power and not from direct costs of treatment.[15,16] Being able to work in a desired occupation may not only have a strong impact on the personal financial situation and on the perception of daily work, but can also be an important health factor. For example, unsatisfactory work situations and poor possibilities for change are associated with increased levels of headache, fatigue and depressed mood.[17]

High amounts of sick leave and impaired work productivity can put affected women under observation and pressure to deliver full performance.[18,19] The rather intimate and gender specific nature of the most common endometriosis symptoms, tends to make affected women feel embarrassed. Consequently, they avoid to discuss these problems with superiors and colleagues, particularly if these are male.[20,21] Due to the invisibility of their disease, they can easily be perceived as malingerers.[20] Therefore, medical professionals need to know about possible difficulties endometriosis can bring on daily working life and professional development; notably as endometriosis affected women repeatedly emphasize their wish for a joint management and guidance from medical professionals, instead of isolated treatment of endometriosis symptoms.[20,22,23] However, research on quantitative and qualitative impairment of working life as the necessary background

for adequate counselling is scarce and relies mainly on interview studies with rather small samples of affected women.[19,20]

Therefore, it was the aim of the present study to investigate (i) career development, (ii) current work performance and (iii) the association between specific disease symptoms and work performance in women diagnosed with endometriosis compared to control women.

Material and Methods

Study design

The study is designed as a multicentre retrospective case-control study. Main outcome measures are the health limitations in career choice and the perceived impact of endometriosis on current work life. Secondary outcome measures investigate the gradual impact of endometriosis on the professional life in association to endometriosis characteristics as well as endometriosis-associated symptoms.

The study has been conducted and reported applying the criteria of the STROBE Statement.[24]

Recruitment

Recruitment of study participants is shown in Figure I. Study participants were recruited between January 2010 and December 2015 at the following hospitals and associated private practices in Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen, Winterthur, Baden and Walenstadt, the Charité Berlin, the Vivantes Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University

Hospital Aachen and the University Hospital Graz. A smaller proportion of the study population (N = 74, 66 of which could be included in the final analysis (13.1% of total case group)) was recruited through different self-help groups for endometriosis patients in Germany. Education level and family income are similar in this cohort and the main group. However, this cohort was significantly older than the hospital group (42.45 ± 6.03 versus 37.02 ± 7.21 years, $p < 0.001$), showed a longer time since primary diagnosis (82.11 ± 8.36 versus 37.20 ± 44.00 months, $p < 0.001$) and presented a significantly higher current stage of disease ($p = 0.013$).

The recruitment of study participants was carried out via direct approach of health care professionals. The questionnaire was explained to the respondent and information about the voluntary nature of participation as well as anonymity of reports and publications of its data was provided. Each participant received a detailed written description of the study and signed informed consent. Participants were given all documents and a return envelope. Control women were recruited either during regular annual gynaecological consultation or stationary hospital stays because of benign gynaecological problems other than endometriosis, and were matched to the patient cohort in respect to age and ethnical background (pair-matching). Each woman diagnosed with endometriosis was matched to a control woman recruited in the same centre for age (± 3 years) and ethnic background.

Inclusion criteria: All study participants had to be between 18 and 50 years. Women diagnosed with endometriosis were included irrespective of disease symptoms but only in case of surgically and histologically confirmed diagnosis. Only data sets with at least 80% of answers for main and secondary outcome measures were included.

Exclusion criteria: Women were excluded in case of current pregnancy and linguistic, mental or psychological impairment that might affect understanding and completing of the questionnaire.

The most frequent reasons reported for not participating were lack of time and the intimate nature of some of the questions. To maximize the return rate women were reminded to complete and return the questionnaire after one and three months.

Questionnaire

The structured self-administered questionnaire contains 390 questions for all participants and 90 additional specific questions for women diagnosed with endometriosis.

It was developed on the background of current literature and clinical experience by specialists for endometriosis of the University Hospital of Zurich and the central board from the endometriosis self-help groups in Germany. The questionnaire focuses on different aspects of quality of life as well as on factors possibly influencing the development of endometriosis. It covers personal demographic data, life style factors, a full gynaecological history and detailed information about the development, symptoms and treatment of endometriosis. Questions about chronic pain concern frequency, duration and intensity and were part of a modified form of the Brief Pain Inventory[25] and the Pain Disability Index[26,27]. Different internationally validated questionnaires investigate aspects of quality of life such as general well-being, sexuality, partnership, and professional life.

The current analysis focused on 26 questions about professional life: A first question addressed highest achieved education level with six preselected answers (lower school education, higher school education, apprenticeship, university degree, no formal education, other). Women had to report the level of their current employment (five preselected answers: full time, part time, full time housekeeping, in education, registered as unemployed), their current own monthly net income (six preselected

answers ranging from none to > 2500 Euros/ > 6000 Swiss francs respectively), their family income and whether they currently worked in their job of choice (yes/ no), how they perceived the level of their qualification for the currently held job (three preselected answers: overqualified, about right, underqualified), the length of their professional experience (< 5 years, 5 - 10 years and > 10 years), their years working with the current employer (< 1 year, 1 - 5 years, 5 - 10 years, > 10 years), and the subjectively perceived influence of health limitations on career choice (not at all, little, medium, strongly, most important factor), as well as the perceived current level of stress on the job (scale from 0 = none to 10 = very strong).

Additional questions focussed on potential consequences of endometriosis on work performance and sick-leave, e.g. missed working time, days worked despite endometriosis symptoms per year, loss of productivity in relation to severity of symptoms and reduction of work time and/ or giving up employment entirely due to endometriosis. Answers to these questions relied on the women's perception of the situation and were only asked to women diagnosed with endometriosis.

Verification of diagnosis and stage of endometriosis

To verify diagnosis, operation reports as well as the histological diagnosis of each patient and each intervention were collected from medical charts. Stage was classified according to the revised Classification of the American Society for Reproductive Medicine (rASRM).[28]

Ethical approval

The study was approved by the Swiss ethics commission as well as by the ethic boards of participating hospitals. This study followed the guidelines of the World Medical Association Declaration of Helsinki 1964, updated in October 2013.

Statistical analysis

Differences in sample characteristics between study groups were computed with either independent sample t-tests for continuous variables or Pearson χ2-tests for categorical variables. To test associations between study groups we conducted a series of either multinomial logistic regression for nominal-scaled outcomes or ordinal logistic regression for ordinal-scaled outcomes. The study group, that is, women with endometriosis versus controls without endometriosis, was always included as the independent predictor variable. The proportion of variance explained based on the study group was indicated by Nagelkerke's pseudo R2. Sample characteristics that differed significantly between study groups were statistically adjusted for by including them simultaneously as covariates. We applied Bonferroni correction to adjust the significance level α for multiple testing. All analyses were conducted with SPSS version 24 for Windows.

Results

Characteristics of study groups and possible confounders

A comparison of socio-epidemiological parameters between women with endometriosis and control women is presented in Table I.

In the subgroups of women having at least one child (26.9% of the case group and 47.1% of the control group) the proportional distribution of having a gainful occupation was as followed: 22.1% (N = 30) of endometriosis affected mothers worked full time versus 23.9% (N = 57) of control mothers, 50.0% (N = 68) of endometriosis affected mothers versus 57.1% (N = 136) of control mothers worked

part time and 27.9% (N = 38) of endometriosis affected mothers versus 18.9% (N = 45) of control mothers did not follow any paid occupation.

Disease chacteristics of the endometriosis group are summarized in Table II.

Parameters of working life

Characteristics of professional activity in women diagnosed with endometriosis and control women are presented in Table III. In the unadjusted analyses, profession of choice, health influences on career choice, adequacy of job qualification, professional experience and stress on the job showed statistically significant differences in both groups. However, except for health influences on career choice (R2 = 0.062), the proportion of variance explained by each factor was very small (all R2 < 0.027). After adjustment for confounders, the associations between a diagnosis of endometriosis and reporting a lower likelihood of working in the job of choice (OR = 0.45), stronger health influences on the selection of the professional activity (OR = 3.08), a higher experience in the current profession (OR = 2.29) and a longer duration of the present employment (OR = 1.65) remained statistically significant.

The intensity of reported health related limitations in career choice was independent of rASRM-stage ($\chi 2$, 16.51, df = 12, p = 0.169), but associated with the occurrence of chronic pain (39.6% vs. 18.3%, $\chi 2$, 34.39, df = 4, p < 0.001) as well as with the frequency of pain ($\chi 2$, 25.62, df = 8, p = 0.001).

Work impairment and compensatory mechanisms

Altogether, 87.6% of the women reported no sick leave due to endometriosis during the month prior to the study period, 10,7% one to three days, 0,7% four to seven days, 0,5% one to two 2 weeks, 0,5% two to four weeks of sick leave without bringing

any medical certificate to their employer. An additional 7,6% had to refrain from work due to endometriosis between two and four weeks and collected a medical certificate (most employers in Switzerland and Germany request a certificate only for more than three days of absence). Asked for the last year, 60.2% of the women diagnosed with endometriosis stated to have never submitted a medical certificate because of their endometriosis. Instead, 13.1% of endometriosis patients used one week or more over time or their vacation when they felt too sick to work. Furthermore, 75.5% of women with endometriosis reported to have gone to work in spite of severe pain during the previous month. A total of 89.2% women affirmed to have worked despite pain in the year prior to the study. Out of these women, 89.8% remarked a loss of work productivity, with 65.1% stating strong or very strong limitations. On days with minimal endometriosis-symptoms still 75.3% felt some loss of productivity.

A minority of women with endometriosis reported working part time (10.3%) or giving up work entirely (5.8%) due to their disease (n = 445).

Influence of endometriosis-associated symptoms on sick leave and productivity loss

We then examined whether different endometriosis symptoms were related to absenteeism and impaired work productivity (Table IV). All four predictor variables were significantly associated with sick leave during the most recent four weeks. The occurrence of chronic pain as well as concomitant psychological symptoms were associated with significantly higher degrees of perceived productivity loss, but effect sizes were modest and accounted for less than 11% of variance explained.

Discussion

Endometriosis, especially in association with chronic pain, interfered with professional activity: Women diagnosed with endometriosis showed a lower likelihood of working in their profession of choice and stronger health-related considerations on their career decisions. They had higher professional experience and had stayed longer in their current employment. Endometriosis-associated symptoms and symptom characteristics were moderately related to sick-leave and work impairment, but in contrast to our expectations, endometriosis was not associated with increased work-related stress levels in multivariate analysis.

Education level and salaries did not differ significantly between case and control group in our study (Table I); a result that has been described previously.[13] Other studies, however, reported serious effects of endometriosis on education, especially on tertiary formation,[8,20]. These contrasting findings might result from differences in study groups, for example with regard to the onset of disease symptoms in relation to education, professional training and professional activity. Many studies report an average age of first symptoms between 20 and 29 years,[6,29-31] i.e. an age in which most women have completed professional training. Other authors reported an earlier onset of disease symptoms,[32] and emphasize that endometriosis in adolescent girls is an underestimated problem.[31,33,34] An additional factor responsible for a different association between endometriosis and education vs. professional performance might be a higher tolerance for sick-leave and impaired energy levels in a school- or university setting compared to paid jobs.

According to the present results women with endometriosis were very successful in their health-related choice of future professions. Although health issues were

important criteria in the initial career choice and women diagnosed with endometriosis do work less often in their desired profession, the resulting choice led to a higher experience in the current profession as well as longer durations working with the same employer (Table III). On one hand, women might prefer to stay with an employer as soon as they found a professional environment adapted to their endometriosis-related needs. On the other hand, they might fear to be unable to find another job and consequently hesitate to change employment. However, our finding that women with endometriosis do not experience higher levels of work-related stress contradicts such assumptions. The fact that women with endometriosis had a lower number of children than the control group may contribute to more stable long-term employment as well as higher professional experience. The association between children and professional activity is also reflected by a higher percentage of women with a paid occupation in women with endometriosis compared to control women. The assumption that the higher number of children of the control women led to more interruptions and reductions of professional activity raises the question why we didn't find higher qualification and consequently higher salaries in women diagnosed with endometriosis. It is possible that professional impairments due to endometriosis and reduction of professional activity due to motherhood balance each other out. This hypothesis is supported by the finding that a very similar percentage of women worked part time in both groups, although women diagnosed with endometriosis more often remained childless. Comparing mothers with and without endometriosis, those with endometriosis more often gave up work entirely. The triple challenge of having children, dealing with a chronic disease like endometriosis and working in a paid occupation might be to stressful for some of these women. Or – considering infertility as a common symptom of endometriosis[4,5] – some women might make

motherhood a priority in their life after years of problems conceiving and quit work for this reason.

However, effect sizes in the direct associations between endometriosis and professional activity were rather small. Altogether, these results show that except the influence of health issues on professional decisions, differences between women diagnosed with endometriosis and control women are minor and a successful long-term professional activity can often be realized despite endometriosis.

Although differences in professional activity between women diagnosed with endometriosis and control women are small, productivity loss[9,15] as well as sick leave[9,10] resulting from endometriosis are relevant issues for many women diagnosed with endometriosis. Average loss of work time per week (absenteeism) due to endometriosis is reported to be between 4.4 and 7.4 hours.[9,10]. In our study, chronic pain, the frequency of pain, fatigue and psychological symptoms were significantly - but with small effect sizes - related to higher amounts of sick leave (Table IV). Productivity loss at work due to endometriosis-related symptoms was described to be high or very high by up to 65% of women in the present study. Struggles to fulfil normal demands of work might further be challenged by therapy side effects, for example by dizziness from strong pain killers.[18,19] Using overtime or vacation to compensate absences from work as well as saving energy for work through reduction of leisure time activities seem to be part of the individual strategies for successful work performance in women with endometriosis in our study and those of others.[32]

As for the relationship between rASRM stage and endometriosis-associated symptoms,[1,3] none of the parameters evaluating professional activity showed any significant association with rARSM stage. In contrast, most outcome measures were

related to the occurrence and frequency of chronic pain, which is supported by other studies on endometriosis[10,15] as well as on other chronic pain conditions such as migraine or fibromyalgia.[35,36] Even if the effect size of pain in this study is small, findings support the relevance of pain management for adequate work performance. Exhaustion, either as a symptom of endometriosis or as a frequent comorbidity,[37] interfered with professional activity in the present as well as in other studies.[1,9]

Several authors reported elevated levels of general[38,39] as well as emotional[21] distress in women diagnosed with endometriosis. Unfortunately, there are no previous reports on work-specific stress in endometriosis affected women. With the specific challenges of a high-quality work performance on the background of a diagnosis of endometriosis, we expected these women to report higher levels of work-related stress than control women. However, this expectation was not met even though women reported to sometimes attend work despite endometriosis-associated pain. As we investigated women whose initial diagnosis was up to 20 years ago, they might meanwhile have found an occupation meeting their needs; and as a result of the often long-term employment, superiors and colleagues might have adapted to their sometimes reduced working ability. Also, the fact that work can be a source of distraction and self-esteem for individuals suffering from a chronic disease,[40] may offset stressful situations. Although the majority of women diagnosed with endometriosis experienced no increased stress levels at work, 16.2% of the women reduced or even gave up work entirely due to endometriosis-associated symptoms, a development that has also been observed by others.[13] Such decisions may result from feeling pressured to reduce or quit work when employers know about a chronic disease as endometriosis.[8,20] More flexible work schedules, a generous policy regarding sick-leave, sufficient breaks, adjusted physical demands, the possibility to

lie down, and bathrooms nearby are estimated to be helpful resources for successful professional performance in women with endometriosis.[19,20]

This study presents one of the largest samples investigating the association between endometriosis and professional life. Study participants were recruited in University, in district hospitals and in private offices in order to collect a representative sample. The pair matching with regard to age and ethnic background allowed to exclude these factors as confounders. A meticulous revision of all operation reports by the same investigator (AKS) ensured a high data quality with regard to diagnosis and classification of endometriosis. The response rate of 64.1% in the case and 35.8% in the control group is in the upper level of comparable studies.[8,9].

Given the method of a self-reported questionnaire in a retrospective design, distortions in the sense of falsely or overly attributing dissatisfaction on the job to endometriosis cannot be excluded. However, such bias would result in overestimation, but the associations found show rather limited effect sizes. By addressing questions on professional activity either on the current situation or the period just prior to study participation we tried to reduce recall bias.

Conclusion

Although endometriosis can have a severe impact on professional activity and development, the majority of women experiences only small limitations of their work performance when health issues are integrated into the choice of a future profession. Disease symptoms as pains and fatigue may interfere with presence at work and the quality of work performance, but most women succeed to integrate endometriosis-associated needs without experiencing a higher degree of work-related stress.

Acknowledgements

We thank all participating women for supporting our study. We gratefully acknowledge the support of Brigitte Alvera, Valerie Bernays, Theodosia Charpidou, Anna Dietlicher, Franziska Graf, Franka Grischott, Elvira Gross, Nicole Kuenzle, Judith Kurmann, Christina Liebermann, Ilona Lukas, Elena Lupi, Sarah Schaerer and Karoline Stojanov in data collection. We thank Salome Looser Ott, PhD, for critical linguistic revision of the manuscript.

Authors roles

MLS: collection of data in Solothurn and Schaffhausen, interpretation of data, drafting and finalization of the manuscript

MPH: statistical analysis, interpretation of data, finalization of manuscript

AKS: investigator, collection of data at site Winterthur, Switzerland, verification of surgical reports, finalization of the manuscript

KG: concept of study, collection of data site Zurich, management databank, finalization of the manuscript

MR: investigator, collection of data at site Berlin, Germany, finalization of the manuscript

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FH: investigator, collection of data at site St. Gallen, Switzerland, finalization of the manuscript

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Tables

Table I: Descriptive statistics and group comparisons

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	P=0.344 [a]
Nationality	Swiss	N=211 (42.2%)	N=285 (57.3%)	P<0.001 [b]
	German	N=244 (48.8%)	N=161 (32.4%)	
	Others	N=45 (9.0%)	N=51 (10.3%)	
Marital status	Married/ Cohabiting	N=420 (83.3%)	N=397 (79.4.6%)	P=0.109 [b]
	Single	N=84 (16.7%)	N=103 (20.6%)	
Pregnancies >24 weeks	0	N=331 (70.6%)	N=245 (50.9%)	P<0.001 [b]
	1	N=83 (17.7%)	N=80 (16.6%)	
	≥2	N=55 (11.7%)	N=156 (32.4%)	
Education level [c]	Low	N=71 (14.4%)	N=74 (14.7%)	P=0.990 [b]
	Medium	N=245 (49.6%)	N=249 (49.4%)	
	High	N=178 (36.0%)	N=181 (35.9%)	
Paid occupation	Full-time	N=248 (49.8%)	N=206 (41.8%)	P=0.016 [b]
	Part-time	N=176 (35.3%)	N=186 (37.7%)	
	None	N=74 (14.9%)	N=101 (20.5%)	

[a] Independent samples t-test
[b] Pearson χ^2-test
[c] Scale: Low="no formal education/ lower school education", Medium="higher school education/ apprenticeship", High="university degree"

Table II: Disease characteristics in women diagnosed with endometriosis

Criteria		Endometriosis Group	N= 505
Time since occurrence of first symptoms (N=474)	less than 1 year	5.49%	26
	1 - 2 years	5.27%	25
	2 -5 years	28.06%	133
	6 -10 years	18.99%	90
	more than 10 years	42.19%	200
rASRM-stage of endometriosis (N=502)	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
Number of endometriosis-related surgical interventions (N=505)	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information	7.33%	37
	Mean ± SD	1.79 ± 1.27	

Table III: Associations between endometriosis and characteristics of professional activity including the proportion of variance explained by the disease

Outcome	Reference category	Unadjusted OR (95% CI)	Adjusted OR** (95% CI)	R^2
Own income	1 point increase [a]	1.26 (0.99; 1.60)	1.09 (0.81; 1.47)	0.004
Profession of choice	Yes	0.47 (0.34; 0.65)*	0.45 (0.31; 0.66)*	0.026
	Partially	0.67 (0.45; 1.00) Ref.	0.65 (0.42; 1.02)	
	No			
Degree of health influences on career choice	1 point increase [b]	2.92 (2.10; 4.04)*	3.08 (2.14; 4.42)*	0.062
Estimation of adequacy of job qualification	too high	1.82 (1.18; 2.80)*	1.47 (0.92; 2.36)	0.011
	too low	1.25 (0.89; 1.77)	1.21 (0.83; 1.77)	
	adequate	Ref.		
Professional experience	1 point increase [c]	1.63 (1.28; 2.07)*	2.29 (1.73; 3.03)*	0.019
Duration of current employment	1 point increase [d]	1.36 (1.07; 1.74)	1.65 (1.26; 2.16)*	0.008
Work-related stress level	1 point increase [e]	1.50 (1.20; 1.89)*	1.17 (0.91; 1.50)	0.014

* Statistically significant at Bonferroni corrected α =0.007

** Adjusted for nationality, number of pregnancies, and occupation

[a] Scale: 1=≤3000 CHF (1000 EUR), 2=3001-6000 CHF (1001-3000 EUR), 3=>6000 CHF (>3000 EUR) per month

[b] Scale: 1="not at all", 2="moderately", 3="strongly"

[c] Scale: 1=<5 years, 2=5-10 years, 3=>10 years

[d] Scale: 1=<1 year, 2=1-5 years, 3=5-10 years, 4=>10 years

[e] Scale: 0="no stress at all" – 10="extreme stress"

Table IV: Association of endometriosis-related symptoms to sick leave and productivity loss in the last four weeks

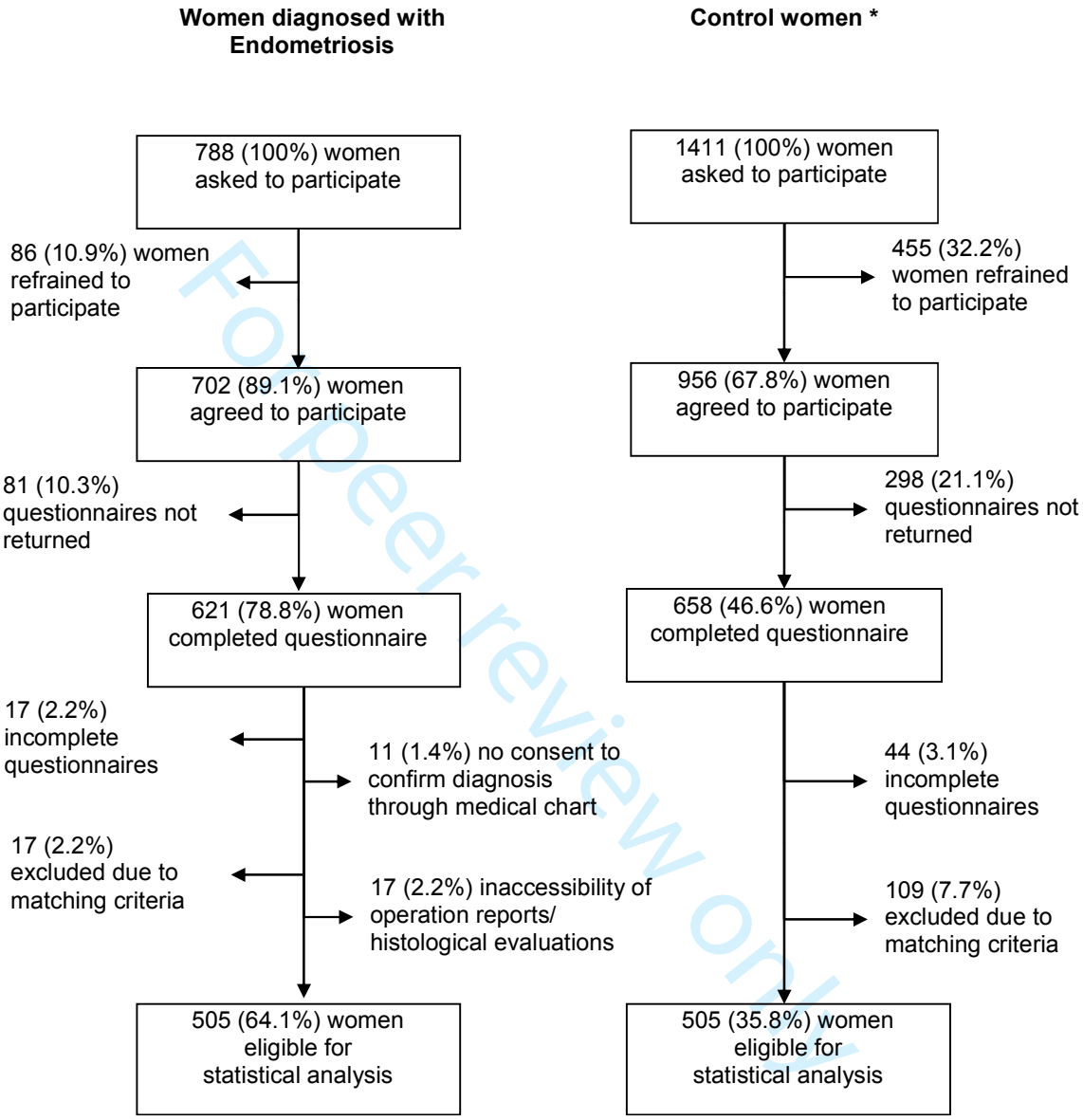
Predictor		Sick leave [a] OR (95% CI)	R^2	Productivity loss [b] OR (95% CI)	R^2
Chronic pain	Yes	3.52 (2.02; 6.13)*	0.072	3.08 (2.11; 4.50)*	0.087
	No	Ref.		Ref.	
Frequency of pain	Daily	2.82 (1.47; 5.39)*	0.053	1.81 (1.05; 3.12)	0.040
	>1 per week	1.40 (0.66; 2.97)		0.76 (0.42; 1.38)	
	≤1 per week	Ref.		Ref.	
Frequency of fatigue	Frequently	3.50 (1.76; 6.94)*	0.073	3.99 (2.49; 6.39)	0.107
	Sometimes	1.15 (0.50; 2.64)		1.44 (0.86; 2.41)	
	Rarely	Ref.		Ref.	
Psychological symptoms	Yes	3.03 (1.77; 5.18)*	0.061	2.90 (1.98; 4.23)*	0.082
	No	Ref.		Ref.	

* Statistically significant at Bonferroni corrected α =0.01

[a] Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

[b] Refers to current maximal impairments; Scale: 1="not at all/ little", 2="moderately/ strong", 3="very strong"

Flow chart I. Recruitment of study participants



* women presenting for routine gynaecological care or benign gynaecological surgery

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8/9*
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Does endometriosis affect professional life? – a matched case-control study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019570.R1
Article Type:	Research
Date Submitted by the Author:	23-Nov-2017
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Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

Does endometriosis affect professional life? – a matched case-control study

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Short title: Endometriosis and professional life

Word count: 4167

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Abstract

Objectives: Endometriosis is a gynaecological disease most commonly causing severe and chronic pelvic pain as well as an impaired quality of life. The aim of this study was to investigate if and how endometriosis affects choices regarding professional life as well as the quality of daily working life.

Design, setting, and participants: In the context of a multicentre case-control study, we collected data from 505 women with surgically/histologically confirmed diagnosis of endometriosis and 505 matched controls. Study participants were recruited prospectively in hospitals and doctors' practices in Switzerland, Germany, and Austria. Using a detailed questionnaire, the study investigated work-life and career choices of study participants.

Main outcome measures: Quantitative and qualitative parameters of professional life as well as associations between endometriosis related symptoms and a reduced ability to work.

Results: Women with endometriosis were less often able to work in their desired profession than women from the control group (OR = 0.45, 95%-CI: 0.31 - 0.66, R^2 = 0.026, $p < 0.001$) and they had to take health-related limitations into consideration in their career decisions to a significantly higher degree than women in the control group (OR = 3.08, 95%-CI: 2.14 - 4.42, R^2 = 0.062, $p < 0.001$). Among women with endometriosis, chronic pain was significantly associated with increased sick leave (OR = 3.52, 95%-CI: 2.02 - 6.13, R^2 = 0.072, $p < 0.001$) as well as with loss of productivity at work (OR = 3.08, 95%-CI: 2.11 - 4.50, R^2 = 0.087, $p < 0.001$).

Conclusions: Endometriosis is associated with impairment of professional life, in particular with regard to career choices. Further research to develop strategies to support endometriosis-affected women in realizing professional opportunities is recommended.

Strengths and limitations of this study

- This study presents one of the largest samples investigating the association between endometriosis and professional activity. It is one of the first studies in this field to provide a matched control group.
- Recruitment of study participants in university hospitals, in district hospitals and in private doctors' practices ensured a representative sample.
- Validation of diagnosis and stage of endometriosis by case reports provided high data quality.
- Given the design of the study (using a self-reported questionnaire answered retrospectively), distortions in the sense of false or excessive attribution of professional dissatisfaction to endometriosis cannot be excluded.
- As we did not investigate diseases or symptoms that may also have had an impact on professional life in the control group, results may be underestimated.

Trial registration number

Clin.trial.gov: Endo_QOL NCT02511626

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors do not have any conflicts of interest.

Data sharing statement

The data set is available on request from the corresponding author.

Key words: Endometriosis, work, professional life, stress, career choice

Introduction

Endometriosis is a gynaecological disease defined by the presence of endometrium-like tissue outside the uterine cavity.[1] The prevalence of the disease among women of reproductive age is estimated to be between 8 and 10%.[2 3]

Women suffering from endometriosis experience most commonly one or more of the following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia, pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea, as well as reduced fertility and chronic fatigue.[4 5] Numerous and severe symptoms, the chronicity of the disease, side effects of therapies as well as diagnostic delays[6 7] significantly affect women's overall quality of life, including professional performance, and place high demands on the treating physicians.[8 9 10] For most patients, available treatment options, such as analgesics, various hormonal therapies, and radical laparoscopy[1] are often not curative and are associated with significant side effects.[8 11]

Consequently, disease symptoms, especially endometriosis-related pain and fatigue, may disturb the development and realization of long-term goals such as a professional career[12] and may make it difficult to meet the demands of a job. About

40% of women with endometriosis report impaired career growth due to endometriosis,[9] and about 50% experience a decreased ability to work due to their chronic disease.[8 13] Differentiated knowledge on the nature of such limitations and in particular on how adjustments to professional life can be made to improve professional performance is currently lacking.

The quality of working life is a major aspect in quality of life overall,[14] which in turn is the most important predictor of total cost of disease.[15] About 66% to 75% of the total costs of endometriosis arise from reduced ability to work and not from direct costs of treatment.[15 16] Being able to work in a desired occupation may not only have a strong impact on a woman's financial situation and on the perception of and attitude toward daily work, but can also be an important health factor. For example, unsatisfactory work and limited possibilities for change are associated with increased levels of headache, fatigue and depressed mood.[17]

Frequent sick leave and reduced work productivity can put affected women under observation by superiors and under greater pressure to deliver full performance.[18 19] The rather intimate and gender-specific nature of the most common endometriosis symptoms tends to make affected women feel embarrassed.[20] Consequently, they avoid discussing endometriosis-related problems with superiors and colleagues, particularly if the superiors and colleagues are male.[20 21] Due to the invisibility of their disease, they can be easily perceived as malingerers.[20] Therefore, medical professionals need to know how the symptoms of endometriosis can affect daily working life and professional development, notably because endometriosis-affected women repeatedly underline their wish for comprehensive information[20 22 23] and advice in managing their disease in daily life,[22 23] instead of isolated treatment of endometriosis symptoms.[20 22 23] However, research on quantitative and qualitative impairment of working life as the necessary background for offering adequate

counselling is scarce and relies mainly on interview-based studies with small samples of affected women[19 20]; there is only one other study that uses a control group.[10] In addition, work-related stress in women diagnosed with endometriosis has not been investigated yet.

Therefore, it was the aim of the present study to investigate parameters of working life of a larger number of endometriosis-affected women, and compare findings with those of a matched control group. We investigated (i) perceived health-related limitations in career decisions; (ii) quality of the current work situation; and (iii) the association between endometriosis-related disease symptoms and work performance.

Material and Methods

Study design

The study is designed as a multicentre case-control study. Main outcome measures are health limitations in career choice as well as quality and stability of the current work situation. Secondary outcome measures investigate the gradual impact of different symptoms as well as localisation of endometriosis on sick leave and loss of productivity. The study has been conducted and reported applying the criteria of the STROBE Statement.[24]

Recruitment

Recruitment of study participants is shown in Figure I. To detect a 10% difference between cases and controls with an alpha of 0.05, a beta of 0.2 and a power of 0.8 a sample size of 387 participants in each group is needed. With the inclusion of 505

participants in both groups we consequently reached very high power, for example 99.1 for the detection of differences in desired profession or 99.7 for health-related limitations in career choice. Study participants were recruited prospectively for a research project on quality of life including professional activity in endometriosis-affected women compared to control women. Study participants were recruited prospectively for a research project on quality of life including professional activity in endometriosis-affected women compared to control women. Recruitment took place between January 2010 and December 2015 at the following hospitals and associated doctors' offices in Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen, Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen, and the University Hospital Graz. In doctors' offices one or several gynecologists work together in a medical unit, district hospitals offer tertiary care associated with a university (= institution with highest academic level).

A smaller segment of the study population (N = 74, 66 of which could be included in the final analysis (13.1% of total case group)) was recruited through different self-help groups for endometriosis patients (in Germany only). Education levels and family incomes in this cohort are similar to those in the main group. However, the women in this cohort were significantly older than those in the hospital group (42.45 ± 6.03 versus 37.02 ± 7.21 years, $p < 0.001$), showed a longer time since primary diagnosis (82.11 ± 8.36 versus 37.20 ± 44.00 months, $p < 0.001$), and presented at the time of the study a significantly higher stage of disease ($p = 0.013$).

The recruitment of study participants was carried out via direct approach by healthcare professionals. The questionnaire was explained to the respondents and information about the voluntary nature of participation as well as anonymity of data in

reports and publications was provided. Each participant received a detailed written description of the study and signed informed consent. Participants were given all documents and a return envelope. Control women were recruited during regular annual or biennial gynaecological consultations, as part of standard healthcare in the three countries where recruitment took place. In addition, women during hospital stays because of temporary mild benign gynaecological problems other than endometriosis were invited to participate in the study. Each control woman was matched to a woman diagnosed with endometriosis for age (± 3 years) and ethnic background, ie Caucasian or not (pair matching).

Inclusion criteria: All study participants had to be between 18 and 50 years old. Women with surgically and histologically diagnosed endometriosis were included irrespective of stage, location of lesions, and severity and profile of symptoms. Only data sets with at least 80% of answers for main and secondary outcome measures were included.

Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic, mental or psychological impairments that might affect their ability to understand and to complete the questionnaire.

The most frequent reasons reported for not participating were lack of time and the intimate nature of some of the questions. To maximize the return rate, women were reminded to complete and return the questionnaire after one month and after three months.

Questionnaire

The structured self-administered questionnaire contained 390 questions for all participants and 90 additional specific questions for women diagnosed with endometriosis. It was developed on the basis of current literature and clinical

experience by endometriosis specialists of the University Hospital of Zurich and the central boards of endometriosis self-help groups in Germany.

All participants received questions regarding demographics; life style; general wellbeing; general, gynaecological, and medical history; childhood experiences; sexuality; partnership; and professional life. Women diagnosed with endometriosis were additionally asked to provide detailed information on the diagnosis and treatment of endometriosis, symptoms of endometriosis, sick leave, and productivity loss due specifically to endometriosis.

The analysis was based on answers to the following questions: nationality (German, Swiss, Austrian, other (with the possibility of entering nationality), age (years), marital status (married/cohabiting/single), highest achieved education level (lower school education, high school education, apprenticeship, university degree, no formal education, other), current own monthly net income (six choices for responses ranging from none to more than 2500 Euros/ none to more than 6000 Swiss francs, respectively), numbers of pregnancies of more than 24 weeks of gestation. Women had to report their levels of current employment (full-time/part-time/full-time housekeeping/student/registered as unemployed) and whether they currently worked in their desired profession (yes/no). This question does not ask about the current place of employment but on the profession itself, eg for a woman who always wanted to be a teacher, is she now able to work as a teacher? They were asked how they perceived their level of qualification for the currently held job (overqualified, about right, under-qualified), length of professional experience (< 5 years, 5 - 10 years, and > 10 years), years working with the current employer (< 1 year, 1 - 5 years, 5 - 10 years, > 10 years), the subjectively perceived influence of health-related limitations on career choice (not at all, little, medium, strongly, exclusively) and perceived current level of stress on the job (scale from 0 = none to 10 = very strong).

The following questions were asked only to women diagnosed with endometriosis: amount of time since first symptoms of endometriosis were noticed (less than 1 year ago/1 year ago/2 - 5 years ago/6 - 10 years ago/more than 10 years ago), date of first diagnosis of endometriosis (month and year), number of surgeries related to endometriosis (1/2-3/4-6/7-10/>10), chronic pain (yes/no), duration of pain (< 1 year/1 - 3 years/4 - 5 years/6 - 10 years/11 - 20 years/> 20 years), frequency of pain (a few times per year/a few times per month/several times per week/once a day/several times a day/permanently), cyclic pain (yes/no), psychological symptoms lasting more than three months estimated by the study participant to be related to endometriosis, such as depressive mood/anxiety/reduced resilience (yes/no), days worked despite pain during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to endometriosis (never, rarely/sometimes/often/very often), sick leave due to symptoms of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/> 12 weeks), estimated loss of productivity due to endometriosis when symptoms are at their maximum or at their minimum respectively (no loss/a little/somewhat/high), reduction of work time due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included dysmenorrhea as well as non-menstrual pelvic pain.)

The study was registered at clinicaltrials.gov (NCT 02511626), where further details on the complete questionnaire are available.

Verification of diagnosis and stage of endometriosis

To verify diagnosis and obtain information about localization of endometriosis lesions, surgical records as well as the histological diagnosis of each patient and each intervention were collected from medical charts. Stage was classified according to the revised Classification of the American Society for Reproductive Medicine (rASRM).[25]

Ethical approval

The study was approved by the Swiss ethics commission as well as by the ethics boards of participating hospitals. This study followed the guidelines of the World Medical Association Declaration of Helsinki 1964, updated in October 2013.

Statistical analysis

Differences in sample characteristics between study groups were computed with either independent sample t-tests for continuous variables or Pearson χ2-tests for categorical variables. To test associations between study groups and characteristics of professional life, we conducted a series of either multinomial logistic regression for nominal-scaled outcomes or ordinal logistic regression for ordinal-scaled outcomes. The study group, ie women with endometriosis as opposed to controls without endometriosis, was always included as the independent predictor variable. The proportion of variance explained based on the study group was indicated by Nagelkerke's pseudo R2. Sample characteristics that differed significantly between study groups were statistically adjusted for by including them simultaneously as covariates. Initially, α was set at 5%. We applied Bonferroni correction to adjust the significance level α for multiple testing. All analyses were conducted with SPSS version 24 for Windows.

Results

Characteristics of study groups and possible confounders

A comparison of socio-epidemiological parameters between women with endometriosis and control women is presented in Table I. Significant variables, eg nationality, pregnancies, and paid employment, were included as covariates in subsequent analyses on case-control effects.

Table I: Descriptive statistics and group comparisons

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 [a]
Nationality	Swiss German Others	N=211 (42.2%) N=244 (48.8%) N=45 (9.0%)	N=285 (57.3%) N=161 (32.4%) N=51 (10.3%)	p<0.001 [b]
Marital status	Married/ Cohabiting Single	N=420 (83.3%) N=84 (16.7%)	N=397 (79.4%) N=103 (20.6%)	p=0.109 [b]
Pregnancies >24 weeks	0 1 ≥2	N=331 (70.6%) N=83 (17.7%) N=55 (11.7%)	N=245 (50.9%) N=80 (16.6%) N=156 (32.4%)	p<0.001 [b]
Education level[c]	Low Medium High	N=71 (14.4%) N=245 (49.6%) N=178 (36.0%)	N=74 (14.7%) N=249 (49.4%) N=181 (35.9%)	p=0.990 [b]
Paid occupation	Full-time Part-time None	N=248 (49.8%) N=176 (35.3%) N=74 (14.9%)	N=206 (41.8%) N=186 (37.7%) N=101 (20.5%)	p=0.016 [b]
Occupation among mothers[d] only	Full-time Part-time None	N= 30 (22.1%) N= 68 (50.0%) N= 38 (27.9%)	N= 57 (23.9%) N= 136 (57.1%) N= 45 (18.9%)	p=0.120 [b]

[a] Independent samples t-test
[b] Pearson χ^2-test
[c] Scale: Low="no formal education/ lower school education", Medium="higher school education/ apprenticeship" High="university degree"
[d] women with at least one pregnancy >24 weeks

Disease characteristics of the endometriosis group are shown in Table II.

Table II: Disease characteristics in women diagnosed with endometriosis

Criteria		**Endometriosis Group**	

		%	N
Time since occurrence of first symptoms (N=474)	< 1 year	5.49%	26
	1-2 years	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	> 10 years	42.19%	200
rASRM-stage of endometriosis (N=502)	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
Number of endometriosis-related surgical interventions (N=505)	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information	7.33%	37
	Mean ± SD	1.79±1.27	
Douglas obliteration (N=503)	Yes	26.6%	134
	No	73.4%	369
Involvement of sacrouterine ligaments (N=503)	Yes	61.4%	309
	No	38.6%	194
Involvement of Douglas (N=503)	Yes	72.0%	362
	No	28.0%	141
Intra-abdominal adhesions (N=504)	Yes	74.8%	377
	No	25.2%	127
Involvement of pelvic wall (N=503)	Yes	74.8%	377
	No	25.2%	127
Involvement of vaginal fornix or septum rectovaginal (N=503)	Yes	12.7%	64
	No	87.3%	439
Endometrioma (N=502)	Yes	49.0%	246
	No	51.0%	256
Chronic pain (N=500)	Yes	58.40%	292
	No	41.60%	208
Duration of chronic pain	Less than 1 year	3.48%	10
	1 - < 3 years	13.59%	39
	3 - < 5 years	17.07%	49
	5 - < 10 years	23.34%	67
	10 - < 20 years	29.27%	84
	≥ 20 years	13.24%	38
Frequency of pain	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
Frequency of endometriosis-related fatigue/ exhaustion	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Frequently	28.14%	141

	Very frequently	22.55%	113
Psychological Symptoms due to endometriosis[a]	Yes	57.24%	261
	No	42.76%	195

[a] depressive mood/ anxiety/ reduced resilience of more than three months

Parameters of working life

Parameters of professional activity in women diagnosed with endometriosis and control women are presented in Table IIIa.

Table IIIa: Parameters of professional activity in the case and the control group

Criteria	Endometriosis group	N	Control group	N
Own net income per month		**480**		**483**
No income	11.25%	54	15.76%	76
<3000 CHF (1000 €)	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500€)	49.17%	236	40.37%	195
>6000 CHF (>2500 €)	14.79%	71	15.32%	74
Desired profession		**488**		**482**
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
Degree of health-related limitations in career choice		**486**		**466**
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
Estimation of adequacy of job qualification		**459**		**453**
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
Professional experience		**487**		**474**
less than 5 years	18.89%	92	32.70%	155
between 5 and 10 years	25.87%	126	21.10%	100
more than 10 years	55.24%	269	46.20%	219
Duration of current employment		**442**		**439**
less than 1 year	14.25%	63	20.27%	89
between 1 and 5 years	40.72%	180	41.69%	183
between 5 and 10 years	22.17%	98	18.91%	83
more than 10 years	22.85%	101	19.13%	84
Work-related stress level		**460**		**465**
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24
3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66

7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

Spearman correlation between professional experience and length of time in the current employment was r = 0.490 (p < 0.001).

Associations between endometriosis and work outcomes after adjustment for age, nationality, number of pregnancies, and occupation are presented in Table IIIb.

Table IIIb: Associations between endometriosis and parameters of professional life including the proportion of variance explained by the disease

Outcome	Reference category	Unadjusted OR (95% CI)	Adjusted OR** (95% CI)	R^2	p**
Own income	1 point increase[a]	1.26 (0.99; 1.60)	1.09 (0.81; 1.47)	0.004	p=0.572
Desired profession	Yes Partially No	0.47 (0.34; 0.65)* 0.67 (0.45; 1.00) Ref.	0.45 (0.31; 0.66)* 0.65 (0.42; 1.02)	0.026	p<0.001
Degree of health-related limitations in career choice	1 point increase[b]	2.92 (2.10; 4.04)*	3.08 (2.14; 4.42)*	0.062	p<0.001
Estimation of adequacy of job qualification	too high too low adequate	1.82 (1.18; 2.80)* 1.25 (0.89; 1.77) Ref.	1.47 (0.92; 2.36) 1.21 (0.83; 1.77)	0.011	p=0.387
Professional experience	1 point increase[c]	1.63 (1.28; 2.07)*	2.29 (1.73; 3.03)*	0.019	p<0.001
Duration of current employment	1 point increase[d]	1.36 (1.07; 1.74)	1.65 (1.26; 2.16)*	0.008	p<0.001
Work-related stress level	1 point increase[e]	1.50 (1.20; 1.89)*	1.17 (0.91; 1.50)	0.014	p=0.210

* Statistically significant at Bonferroni corrected α=0.007
** Adjusted for age, time since diagnosis, nationality, number of pregnancies, and occupation
[a] Scale: 1=≤3000 CHF (1000 EUR), 2=3001-6000 CHF (1001-3000 EUR), 3=>6000 CHF (>3000 EUR) per month
[b] Scale: 1="not at all", 2="moderately", 3="strongly"
[c] Scale: 1=<5 years, 2=5-10 years, 3=>10 years
[d] Scale: 1=<1 year, 2=1-5 years, 3=5-10 years, 4=>10 years
[e] Scale: 0="no stress at all" – 10="extreme stress"

Results of the main outcome measures are highly significant. However, except for health influences on career choice (R2 = 0.062), the proportion of variance explained

by each factor was small (all R2 < 0.027). Excluding participants who are members of self-help groups did not alter the results, except that the multivariate analysis for professional experience was attenuated to OR=1.49 (p = 0.003), whereas the adjusted association with duration of the current employment was diminished to an insignificant OR = 1.17 (p = 0.231).

The intensity of reported health-related limitations in career choice was independent from rASRM-stage (χ2, 16.51, df = 12, p = 0.169), but associated with the occurrence of chronic pain (χ2, 34.39, df = 4, p < 0.001) as well as with the frequency of pain (χ2, 25.62, df = 8, p = 0.001).

Chronic pain was also associated with higher levels of stress at work, even if the difference of means was rather small (6.61 vs 5.47, SD = 2.39/ 2.49, p < 0.001).

Intraoperative findings of spread of endometriosis lesions showed varying associations with health-related limitations in career choice: having endometriosis lesions at the pelvic wall (χ2, 11.14, df = 4, p = 0.025) or in the sacrouterine ligaments (χ2, 13.51, df = 4, p = 0.009) was significantly associated with greater limitations in career choice, while such an outcome could not be found for localization in the vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50, SD = 2.46/ 2.48, p = 0.001), but not with other intraoperative findings.

Work impairment and compensatory mechanisms

Asked about the amount of sick leave due to endometriosis during the last month, 78.1% of the women of the case group reported no sick leave, 8.5% reported one to

three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and 8.1% reported two to four weeks.

Altogether, 13.1% of endometriosis patients used one week or more of overtime or vacation when they felt too sick to work. Furthermore, 75.5% of women with endometriosis reported to have gone to work during the previous month in spite of severe pain. Asked about the previous year, 89.2% of women affirmed to have worked despite pain. Out of these women, 89.8% noted a loss of work productivity, with 65.1% reporting strong or very strong limitations when symptoms were severe. On days with minimal endometriosis symptoms, 75.3% still felt some degree of loss of productivity.

A minority of women with endometriosis reported working part time (10.3%) or giving up work entirely (5.8%) due to their disease (n = 445).

Association of endometriosis-related symptoms with sick leave and productivity loss

We then examined whether different endometriosis symptoms were related to absenteeism and impaired work productivity (Table IV).

Table IV: Association of endometriosis-related symptoms to sick leave and productivity loss in the last month

Predictor		**Sick leave** [a]			**Productivity loss** [b]		
		OR (95% CI)**	**R^2**	**p**	**OR** (95% CI)**	**R^2**	**p****
Chronic pain	Yes No	3.52 (2.02; 6.13)* Ref.	0.072	p<0.001	3.08 (2.11; 4.50)* Ref.	0.087	p<0.001
Frequency of pain	Daily >1 per week ≤1 per week	2.82 (1.47; 5.39)* 1.40 (0.66; 2.97) Ref.	0.053	p=0.002	1.81 (1.05; 3.12) 0.76 (0.42; 1.38) Ref.	0.040	p=0.032
Frequency of fatigue	Frequently Sometimes Rarely	3.50 (1.76; 6.94)* 1.15 (0.50; 2.64) Ref.	0.073	p<0.001	3.99 (2.49; 6.39) 1.44 (0.86; 2.41) Ref.	0.107	p<0.001

Psychological symptoms [c]	Yes No	3.03 (1.77; 5.18)* Ref.	0.061	p<0.001	2.90 (1.98; 4.23)* Ref.	0.082	p<0.001

* Statistically significant at Bonferroni corrected α=0.01
** Adjusted for age and time since diagnosis
[a] Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days
[b] Refers to current maximal impairments; Scale: 1="not at all/ little", 2="moderately/ strong", 3="very strong"
[c] depressive mood/ anxiety/ reduced resilience of more than three months

All four predictor variables were significantly associated with sick leave during the previous four weeks. The occurrence of chronic pain as well as concomitant psychological symptoms were associated with significantly higher degrees of perceived productivity loss, but the extent of the effect was modest and the effect accounted for less than 11% of variance explained. Including age and time since diagnosis as potential confounders did not alter the results. Likewise, the factor of different localisations of endometriosis was not associated with sick leave or productivity loss (all $p > 0.05$).

Discussion

Endometriosis is associated with impairment of professional activity: women diagnosed with endometriosis showed a lower likelihood of working in their desired profession and stronger health-related limitations in their career decisions. In contrast, they had professional experience of longer durations. All of these main outcomes were not reported previously and open new insights into the professional life of women with endometriosis.

Endometriosis-associated symptoms and symptom characteristics were moderately related to sick leave and loss of productivity, but in contrast to our expectations, endometriosis was not associated with increased work-related stress levels.

Education level and salaries did not differ significantly between case and control groups (Table I); this is a result that has been described previously.[13] Other studies, however, reported serious effects of endometriosis on education level, especially on tertiary formation.[8 20] These contrasting findings might result from differences in study groups, eg with regard to the onset of disease symptoms in relation to education, professional training and professional activity. Many studies report an average age of first symptoms between 20 and 29 years,[6 26-28] ie an age at which most women have completed professional training. Other authors reported an earlier onset of disease symptoms,[29] and emphasized that endometriosis in adolescent girls was an underestimated problem.[28 30 31] An additional factor responsible for a different association between endometriosis and education vs. professional performance might be a higher tolerance for sick leave and impaired energy levels in a school or university setting compared to in paid employment.

Health issues are important criteria in career choice, and women diagnosed with endometriosis do work less often in their desired profession. However, women with endometriosis reported a higher quality of experience in the current profession (Table IIIb). Professional experience and the length of time a woman is working with the current employer are highly correlated, and the difference between groups for time with the same employer remained no longer significant when women attending a self-help group were excluded. These results can be interpreted positively in the sense that women with endometriosis were successful in carefully choosing a long-term profession. The lower number of children in women with endometriosis may also contribute to a professional experience of longer duration.

Several authors reported elevated levels of general[32 33] as well as emotional[21] distress in women diagnosed with endometriosis. This first study on work-specific stress in endometriosis affected women produced results in contrast to our expectations. Even though women reported that they sometimes went to work despite endometriosis-associated pain, women with endometriosis did not experience higher work-related stress levels than the control women; but within the group of women with endometriosis, those with chronic pain reported significantly higher work-related stress than those without pain. We investigated women whose initial diagnosis was up to 20 years ago; these women may have meanwhile found an occupation meeting their needs, and superiors and colleagues may have adapted to their sometimes reduced availability for work. Also, the fact that work can be a source of distraction and of self-esteem for individuals suffering from a chronic disease[34] may offset stressful situations.

According to our results and those of others,[29] women affected by endometriosis compensate for their health-related restrictions at work by using overtime or vacation for absences as well as by saving energy for work through reduction of leisure time activities.

Despite these personal efforts to adapt to an adverse situation, productivity loss[9 15] and sick leave[9 10] are relevant issues for many women diagnosed with endometriosis. Average loss of work time per week (absenteeism) due to endometriosis is reported to be between 4.4 and 7.4 hours.[9 10] In our study, chronic pain, the frequency of pain, fatigue, and psychological symptoms, such as self-reported depression and anxiety, were significantly - but with small effect sizes - related to taking more sick leave (Table IV). Productivity loss at work due to endometriosis-related symptoms was described to be high or very high – depending on the current severity of symptoms –

by up to 65% of women in the present study. Struggles to fulfil normal demands of work might be exacerbated by the side effects of treatment, for example by dizziness from strong pain killers.[18 19] Although, the majority of women affected with endometriosis seemed to be able to compensate for disease-related difficulties at work and to realize successful long-term professional activity, 16.2% of the women nevertheless reduced or even gave up work entirely due to endometriosis-related symptoms; this is a situation that has been observed also by others.[13] Furthermore, a very similar percentage of women with endometriosis and control women worked part time, even though women diagnosed with endometriosis remained childless more often. Such decisions may result from feeling pressured to reduce or quit work when employers know about a chronic disease such as endometriosis.[8 20] More flexible work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted physical demands, the possibility to lie down, and the existence of bathrooms nearby are seen to be helpful resources for successful professional performance in women with endometriosis.[19 20]

As for the relationship between rASRM stage and endometriosis-associated symptoms,[1 3] none of the parameters evaluating professional activity showed any significant association with rARSM stage. Testing the association between different intraoperative findings of endometriotic lesions and work outcomes showed inconsistent results. In contrast, most outcome measures were related to the occurrence and frequency of chronic pain; this result is supported by other studies on endometriosis,[10 15] as well as on other chronic pain conditions such as migraine or fibromyalgia.[35 36] Even if the effect size of pain on work in this study is limited, findings support the relevance of pain management for satisfactory work

performance. Exhaustion, either as a symptom of endometriosis or as a frequent comorbidity,[37] interfered with professional activity in this as well as in other studies.[1 9] In summary, women with endometriosis strive for normality at their work place, even if it is associated with reduced professional flexibility or with giving up the desire for another profession.

This study presents one of the largest samples investigating the association between endometriosis and professional life and it is one of the very few studies providing a control group. Study participants were recruited in university hospitals, in district hospitals and in doctors' practices in order to collect a representative sample. The pair matching with regard to age and ethnic background reduced the confounding effect of these factors. A meticulous review of all surgical records by the same investigator (AKS) ensured high data quality with regard to diagnosis and classification of endometriosis. The response rate of 64.1% in the case group is in the upper level of comparable studies,[8 9] whereas the response rate of 35.8% in the control group is comparatively low. We cannot exclude that women with a particularly high work load refrained from study participation; however, such an effect is equally relevant in women diagnosed with endometriosis and in controls. The higher response rate in women with endometriosis supports the fact that such an association does not represent a particular problem for members in this group.

Given the methodology of a self-reported questionnaire answered retrospectively, distortions in the sense of falsely or overly attributing dissatisfaction on the job to endometriosis cannot be excluded. By addressing questions on professional activity either current or in the period just prior to study participation, we tried to reduce recall bias. As we included only patients with a confirmed diagnosis of endometriosis, and as such a confirmation can be provided only by surgery, there may be referral bias.

For example, affected but asymptomatic women and symptomatic women who do not have access to or refused surgery might have been excluded. In contrast, asymptomatic women with endometriosis might have been included in the control group which would result in underestimation of results. As we have no differentiated information on symptoms resulting from diseases other than endometriosis, in both groups further confounders might be present; this would also result in underestimation of our findings. A comparison group for the questions of sick leave and productivity loss at work would have been beneficial. However, analysis of gradual impact of different endometriosis-related symptoms on these two outcomes allowed for indirect conclusions on the association between endometriosis and reduced working ability, as well as basic data to design future studies.

Conclusion

Even if most measured effect sizes of associations between endometriosis and individual parameters of working life were small, the study confirms a burdensome influence of the disease on the working life of women affected by endometriosis. Therefore, medical support should address such issues in order to support women in adjusting their professional choices and professional development to individual endometriosis-related conditions.

Acknowledgements

We thank all participating women for supporting our study. We gratefully acknowledge the support of Brigitte Alvera, Valerie Bernays, Theodosia Charpidou, Anna Dietlicher, Franziska Graf, Franka Grischott, Elvira Gross, Nicole Kuenzle,

Judith Kurmann, Christina Liebermann, Ilona Lukas, Elena Lupi, Sarah Schaerer, and Karoline Stojanov in data collection. We thank Salome Looser Ott, PhD, and Kathryn Imboden for critical linguistic revision of the manuscript.

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MPH: statistical analysis, interpretation of data, finalization of manuscript

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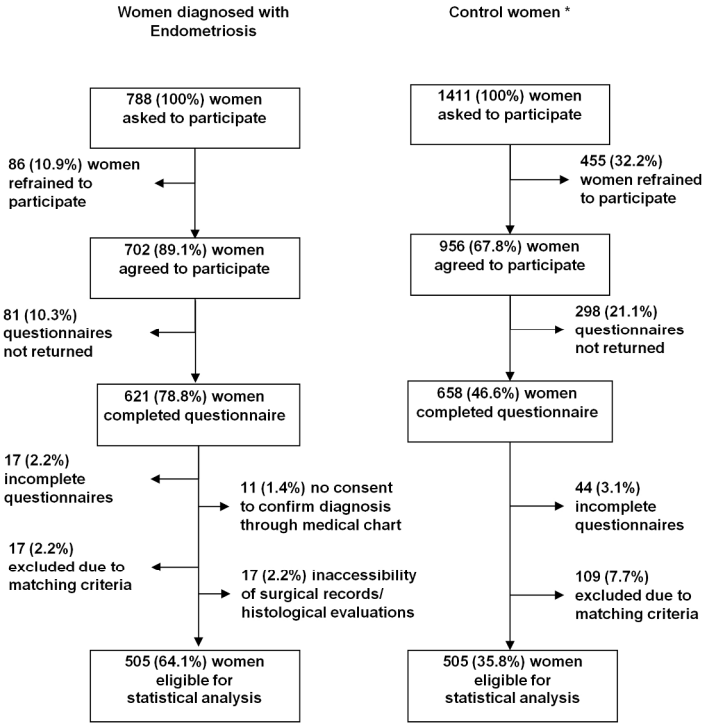
Figure legends

Fig 1.: Recruitment of study participants

Flow chart I. Recruitment of study participants



* women presenting for routine gynaecological care or benign gynaecological surgery

190x274mm (284 x 284 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8/9*
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Does endometriosis affect professional life? – a matched case-control study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019570.R2
Article Type:	Research
Date Submitted by the Author:	03-Mar-2018
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Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

Does endometriosis affect professional life? – a matched case-control study

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Short title: Endometriosis and professional life

Word count: 4167

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Abstract

Objectives: Endometriosis is a gynaecological disease most commonly causing severe and chronic pelvic pain as well as an impaired quality of life. The aim of this study was to investigate if and how endometriosis affects choices regarding professional life as well as the quality of daily working life.

Design, setting, and participants: In the context of a multicentre case-control study, we collected data from 505 women with surgically/histologically confirmed diagnosis of endometriosis and 505 matched controls. Study participants were recruited prospectively in hospitals and doctors' practices in Switzerland, Germany, and Austria. Using a detailed questionnaire, the study investigated work-life and career choices of study participants.

Main outcome measures: Associations between endometriosis/ disease symptoms and limitations in career development as well as ability to work.

Results: Women with endometriosis were less often able to work in their desired profession than women from the control group (adjusted OR=1.84, 95%-CI: 1.15-2.94, R^2=0.029, p=0.001 and they had to take health-related limitations into consideration in their career decisions to a significantly higher degree than women in the control group (aOR=4.79, 95%-CI: 2.30-9.96, R^2=0.063, p<0.001). Among women with endometriosis, chronic pain was significantly associated with increased sick leave (OR=3.52, 95%-CI: 2.02-6.13, R^2=0.072, p<0.001) as well as with loss of productivity at work (OR=3.08, 95%-CI: 2.11-4.50, R^2=0.087, p<0.001).

Conclusions: Endometriosis is associated with impairment of professional life, in particular with regard to career choices. Further research to develop strategies to

support endometriosis-affected women in realizing professional opportunities is recommended.

Strengths and limitations of this study

This study presents one of the largest samples investigating the association between endometriosis and professional activity. It is one of the first studies in this field to provide a matched control group.

Recruitment of study participants in university hospitals, in district hospitals and in private doctors' practices ensured a representative sample.

Validation of diagnosis and stage of endometriosis by case reports provided high data quality.

Given the design of the study (using a self-reported questionnaire answered retrospectively), distortions in the sense of false or excessive attribution of professional dissatisfaction to endometriosis cannot be excluded.

As we did not investigate diseases or symptoms that may also have had an impact on professional life in the control group, results may be underestimated.

Trial registration number

Clin.trial.gov: Endo_QOL NCT02511626

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors do not have any conflicts of interest.

Data sharing statement

The data set is available on request from the corresponding author.

Key words: Endometriosis, work, professional life, stress, career choice

Introduction

Endometriosis is a gynaecological disease defined by the presence of endometrium-like tissue outside the uterine cavity.[1] The prevalence of the disease among women of reproductive age is estimated to be between 8 and 10%.[2 3]

Women suffering from endometriosis experience most commonly one or more of the following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia, pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea, as well as reduced fertility and chronic fatigue.[4 5] Numerous and severe symptoms, the chronicity of the disease, side effects of therapies as well as diagnostic delays[6 7] significantly affect women's overall quality of life, including professional performance, and place high demands on the treating physicians.[8 9 10] For most patients, available treatment options, such as analgesics, various hormonal therapies, and radical laparoscopy[1] are often not curative and are associated with significant side effects.[8 11]

Consequently, disease symptoms, especially endometriosis-related pain and fatigue, may disturb the development and realization of long-term goals such as a professional career[12] and may make it difficult to meet the demands of a job. About 40% of women with endometriosis report impaired career growth due to endometriosis,[9] and about 50% experience a decreased ability to work due to their chronic disease.[8 13] Differentiated knowledge on the nature of such limitations and in

particular on how adjustments to professional life can be made to improve professional performance is currently lacking.

The quality of working life is a major aspect in quality of life overall,[14] which in turn is the most important predictor of total cost of disease.[15] About 66% to 75% of the total costs of endometriosis arise from reduced ability to work and not from direct costs of treatment.[15 16] Being able to work in a desired occupation may not only have a strong impact on a woman's financial situation and on the perception of and attitude toward daily work, but can also be an important health factor. For example, unsatisfactory work and limited possibilities for change are associated with increased levels of headache, fatigue and depressed mood.[17]

Frequent sick leave and reduced work productivity can put affected women under observation by superiors and under greater pressure to deliver full performance.[18 19] The rather intimate and gender-specific nature of the most common endometriosis symptoms tends to make affected women feel embarrassed.[20] Consequently, some women may avoid discussing endometriosis-related problems with superiors and colleagues, particularly if the superiors and colleagues are male.[20 21] Due to the invisibility of their disease, women can be easily perceived as malingerers.[20] Therefore, medical professionals need to know how the symptoms of endometriosis can affect daily working life and professional development, notably because endometriosis-affected women repeatedly underline their wish for comprehensive information[20 22 23] and advice in managing their disease in daily life,[22 23] instead of isolated treatment of endometriosis symptoms.[20 22 23] A better understanding of endometriosis and its impacts on any aspect of life - including professional activity - not only by medical professionals but also in society and politics would help affected women and their families to reduce negative consequences of the disease. However, research on quantitative and qualitative impairment of working life as the necessary

background for offering adequate support and interventions is scarce and relies mainly on interview-based studies with small samples of affected women[19 20]; there is only one other study that uses a control group.[10] In addition, work-related stress in women diagnosed with endometriosis has not been investigated yet.

Therefore, it was the aim of the present study to investigate parameters of working life of a larger number of endometriosis-affected women, and compare findings with those of a matched control group. We investigated (i) perceived health-related limitations in career decisions; (ii) quality of the current work situation; and (iii) the association between endometriosis-related disease symptoms and work performance.

Material and Methods

Study design

The study is designed as a multicentre case-control study. Main outcome measures are health limitations in career choice as well as quality and stability of the current work situation. Secondary outcome measures investigate the impact of different symptoms as well as localisation of endometriosis on sick leave and loss of productivity. The study has been conducted and reported applying the criteria of the STROBE Statement.[24]

Recruitment

Recruitment of study participants is shown in Figure I. To detect a 10% difference between cases and controls with an alpha of 0.05, and a power of 0.8 a sample size of 387 participants in each group is needed. With the inclusion of 505 participants in

both groups we consequently reached very high power, for example 99.1 for the detection of differences in desired profession or 99.7 for health-related limitations in career choice. Study participants were recruited prospectively for a research project on quality of life including professional activity in endometriosis-affected women compared to control women. Recruitment took place between January 2010 and December 2015 at the following hospitals and associated doctors' offices in Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen, Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen, and the University Hospital Graz. In doctors' offices one or several gynecologists work together in a medical unit; district hospitals offer tertiary care associated with a university.

Healthcare professionals carried out the recruitment of all study participants via direct approach. The study was explained to the respondents and information about the voluntary nature of participation as well as anonymity of data in reports and publications was provided. Each participant received a detailed written description of the study and signed informed consent. Participants were given all documents and a return envelope.

Inclusion criteria: All study participants had to be between 18 and 50 years old. For the case group, women with surgically and histologically diagnosed endometriosis were included irrespective of stage, location of lesions, and severity and profile of symptoms. Only data sets with at least 80% of answers for main and secondary outcome measures were included.

Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic, mental or psychological impairments that might affect their ability to understand and

to complete the questionnaire.

The most frequent reasons reported for not participating were lack of time and the intimate nature of some of the questions. To maximize the return rate, women were reminded to complete and return the questionnaire after one month and after three months.

A smaller segment of the case group (N=74, 66 of which could be included in the final analysis (13.1% of total case group)) was recruited through different self-help groups for endometriosis patients (in Germany only). Education levels and family incomes in this cohort are similar to those in the main group. However, the women in this cohort were significantly older than those in the hospital group (42.45±6.03 versus 37.02±7.21 years, $p<0.001$), showed a longer time since primary diagnosis (82.11±8.36 versus 37.20±44.00 months, $p<0.001$), and presented at the time of the study a significantly higher stage of disease ($p=0.013$).

Control women were recruited during regular annual or biennial gynaecological consultations, as part of standard healthcare in the three countries where recruitment took place. In addition, women during hospital stays because of temporary mild benign gynaecological problems other than endometriosis were invited to participate in the study. Each control woman was matched to a woman diagnosed with endometriosis for age (±3 years) and ethnic background, i.e. Caucasian or not (pair matching).

Questionnaire

The structured self-administered questionnaire for the total study on quality of life contained 390 questions for all participants and 90 additional specific questions for women diagnosed with endometriosis. It is structured in different chapters, one of which is professional life. Further chapters covered questions regarding life style;

general wellbeing; general, gynaecological, and medical history; childhood experiences; sexuality and partnership. Women diagnosed with endometriosis were additionally asked to provide detailed information on the diagnosis and treatment of endometriosis, symptoms of endometriosis, sick leave, and productivity loss due specifically to endometriosis. Wherever possible we used internationally validated questionnaires. Modified versions of the Brief Pain Inventory[25] and the Pain Disability Index[26 27] served to evaluate pain. For several questions about professional life as for occupation, sick leave and productivity loss, we used similar reporting methods the WPAI[28] suggests, but extended the time period of reporting from only seven days in the WPAI to four weeks and one year. Level of education was measured with defined categories following the recommendation to use meaningful benchmarks of educational attainment rather than a continuous scale in years.[29] In order to capture the professional situation of women diagnosed with endometriosis as close to reality as possible a interdisciplinary research team including specialists for minimally invasive endometriosis-surgery, for gynaecological endocrinology and for gynaeco-psychosomatic medicine added their clinical experience and evaluated systematically what they had learned from individual patients. On this background specific questions like on working despite pain or on using overtime or holidays to compensate for sick leave were added. The first version of our questions on professional activity was than revised by the governing body of the German self-help groups in order to map the questions to the situations reported by women with endometriosis and to avoid using questions, which do not correctly depict the specific situation in the context of endometriosis.

The analysis presented in this paper was based on answers to the following questions asked to the case as well as to the control group: nationality (German, Swiss, Austrian, other [with the possibility of entering nationality]), age (years),

marital status (married/cohabiting/single), highest achieved education level (lower school education, high school education, apprenticeship, university degree, no formal education, other), current own monthly net income (six choices for responses ranging from none to >2500 Euros for participants in Germany and Austria and from none to >6000 Swiss francs for participants in Switzerland), numbers of pregnancies of more than 24 weeks of gestation. Women were asked to report their levels of current employment (full-time/part-time/full-time housekeeping/student/registered as unemployed) and whether they currently worked in their desired profession (yes/no). This question does not ask about the current place of employment but on the profession itself, e.g. for a woman who always wanted to be a teacher, is she now able to work as a teacher? They were asked how they perceived their level of qualification for the currently held job (overqualified, about right, under-qualified), length of professional experience (<5 years, 6-10 years, and >10 years), years working with the current employer (<1 year, 1-5 years, 6-10 years, >10 years), the subjectively perceived influence of health-related limitations on career choice (not at all, little, medium, strongly, exclusively) and perceived current level of stress on the job (scale from 0=none to 10=very strong).

The analysis presented in this paper further used the following questions asked only to women diagnosed with endometriosis: Amount of time since first symptoms of endometriosis were noticed (<1 year ago/1 year ago/2-5 years ago/6-10 years ago/>10 years ago), date of initial diagnosis of endometriosis (month and year), number of surgeries related to endometriosis (1/2/3/4/5/6 or more), chronic pain (yes/no), duration of pain (<1 year/1-3 years/4-5 years/6-10 years/11-20 years/>20 years), frequency of pain (a few times per year/a few times per month/several times per week/once a day/several times a day/permanently), cyclic pain (yes/no), psychological symptoms lasting more than three months estimated by the study

participant to be related to endometriosis, such as depressive mood/anxiety/reduced resilience (yes/no), days worked despite pain during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to endometriosis (never/rarely/sometimes/often/very often), sick leave due to symptoms of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/>12 weeks), estimated loss of productivity due to endometriosis when symptoms are at their maximum or at their minimum respectively (no loss/a little/somewhat/high), reduction of work time due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included cyclic as well as non-cyclic pelvic pain.)

The study was registered at clinicaltrials.gov (NCT 02511626), where further details on the complete questionnaire are available.

Verification of diagnosis and stage of endometriosis

To verify diagnosis and obtain information about localization of endometriosis lesions, surgical records as well as the histological diagnosis of each patient and each intervention were collected from medical charts. Stage was classified according to the revised Classification of the American Society for Reproductive Medicine (rASRM).[30]

Ethical approval

The study was approved by the Swiss ethics commission as well as by the ethics boards of participating hospitals. This study followed the guidelines of the World Medical Association Declaration of Helsinki 1964, updated in October 2013.

Patient and Public Involvement statement

Questions for this study were selected in cooperation with endometriosis self-help groups. Other than in the self-help groups patients were not involved in the recruitment and conduct of the study. All interested study participants receive the publications resulting from the study. Publications are also sent to the governing body of the self-help groups.

Statistical analysis

Differences in sample characteristics between study groups were computed with either independent sample t-tests for continuous variables or Pearson χ2-tests for categorical variables. To test associations between study groups and characteristics of professional life, we conducted a series of binomial logistic regression. The study group, i.e. women with endometriosis as opposed to controls without endometriosis, was included as the dependent variable. To test association between symptoms of endometriosis and work outcomes in women with endometriosis, we conducted a series of ordinal logistic regression, entering work outcomes as the dependent variable. The proportion of variance explained based on the study group was indicated by Nagelkerke's pseudo R^2. Sample characteristics that differed significantly between study groups were statistically adjusted for by including them simultaneously as covariates. Initially, α was set at 5%, but we applied Bonferroni correction to adjust the significance level α for multiple testing. All analyses were conducted with SPSS version 24 for Windows.

Results

Characteristics of study groups and possible confounders

A comparison of socio-epidemiological parameters between women with endometriosis and control women is presented in Table I. Significant variables, eg nationality, pregnancies, and paid employment, were included as covariates in subsequent analyses on case-control effects.

Table I: Descriptive statistics and group comparisons

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 [a]
Nationality	Swiss German Others	N=211 (42.2%) N=244 (48.8%) N=45 (9.0%)	N=285 (57.3%) N=161 (32.4%) N=51 (10.3%)	p<0.001 [b]
Marital status	Married/ Cohabiting Single	N=420 (83.3%) N=84 (16.7%)	N=397 (79.4%) N=103 (20.6%)	p=0.109 [b]
Pregnancies >24 weeks	0 1 ≥2	N=331 (70.6%) N=83 (17.7%) N=55 (11.7%)	N=245 (50.9%) N=80 (16.6%) N=156 (32.4%)	p<0.001 [b]
Education level[c]	Low Medium High	N=71 (14.4%) N=245 (49.6%) N=178 (36.0%)	N=74 (14.7%) N=249 (49.4%) N=181 (35.9%)	p=0.990 [b]
Paid occupation	Full-time Part-time None	N=248 (49.8%) N=176 (35.3%) N=74 (14.9%)	N=206 (41.8%) N=186 (37.7%) N=101 (20.5%)	p=0.016 [b]
Occupation among mothers[d] only	Full-time Part-time None	N=30 (22.1%) N=68 (50.0%) N=38 (27.9%)	N=57 (23.9%) N=136 (57.1%) N=45 (18.9%)	p=0.120 [b]

Note

[a] Independent samples t-test

[b] Pearson χ^2-test

[c] Scale: Low="no formal education/lower school education", Medium="higher school education/apprenticeship", High="university degree"

[d] women with at least one pregnancy >24 weeks

Disease characteristics of the endometriosis group are shown in Table II.

Table II: Disease characteristics in women diagnosed with endometriosis

Criteria		**Endometriosis Group**	

		%	N
Time since occurrence of first symptoms (N=474)	<1 year	5.49%	26
	1 year	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	>10 years	42.19%	200
rASRM-stage of endometriosis (N=502)	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
Number of endometriosis-related surgical interventions (N=505)	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information[a]	7.33%	37
	Mean±SD	1.79±1.27	
Douglas obliteration (N=503)	Yes	26.6%	134
	No	73.4%	369
Involvement of sacrouterine ligaments (N=503)	Yes	61.4%	309
	No	38.6%	194
Involvement of Douglas (N=503)	Yes	72.0%	362
	No	28.0%	141
Intra-abdominal adhesions (N=504)	Yes	74.8%	377
	No	25.2%	127
Involvement of pelvic wall (N=503)	Yes	74.8%	377
	No	25.2%	127
Involvement of vaginal fornix or septum rectovaginal (N=503)	Yes	12.7%	64
	No	87.3%	439
Endometrioma (N=502)	Yes	49.0%	246
	No	51.0%	256
Chronic pain (N=500)	Yes	58.40%	292
	No	41.60%	208
Duration of chronic pain	<1 year	3.48%	10
	1-3 years	13.59%	39
	4-5 years	17.07%	49
	6-10 years	23.34%	67
	11-20 years	29.27%	84
	>20 years	13.24%	38
Frequency of pain	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
Frequency of endometriosis-related fatigue/ exhaustion	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Often	28.14%	141

	Very often	22.55%	113
Psychological Symptoms due to endometriosis[b]	Yes	57.24%	261
	No	42.76%	195

Note

[a] question not answered but diagnosis of endometriosis confirmed with at least one surgical record

[b]depressive mood/anxiety/reduced resilience of more than three months

Parameters of working life

Parameters of professional activity in women diagnosed with endometriosis and control women are presented in Table IIIa.

Table IIIa: Parameters of professional activity in the case and the control group

Criteria	Endometriosis group	N	Control group	N
Own net income per month		**480**		**483**
No income	11.25%	54	15.76%	76
<3000 CHF (1000 EUR)[a]	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500 EUR)[a]	49.17%	236	40.37%	195
>6000 CHF (>2500 EUR)[a]	14.79%	71	15.32%	74
Desired profession		**488**		**482**
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
Degree of health-related limitations in career choice		**486**		**466**
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
Estimation of adequacy of job qualification		**459**		**453**
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
Professional experience		**487**		**474**
<5 years	18.89%	92	32.70%	155
5-10 years	25.87%	126	21.10%	100
>10 years	55.24%	269	46.20%	219
Duration of current employment		**442**		**439**
<1 year	14.25%	63	20.27%	89
1-5 years	40.72%	180	41.69%	183
6-10 years	22.17%	98	18.91%	83
>10 years	22.85%	101	19.13%	84
Work-related stress level		**460**		**465**
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24

3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66
7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

Note

[a] different income classes in Switzerland and Germany/ Austria

Spearman correlation between professional experience and length of time in the current employment was r=0.490 (p<0.001).

Associations between endometriosis and work outcomes are presented in Table IIIb. In the adjusted analysis, all predictor variables plus nationality, occupation and number of pregnancies were included simultaneously as covariates.

Table IIIb: Associations between endometriosis and parameters of professional life including the proportion of variance explained by the disease

Predictor	Reference category	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[b]	Pseudo R^2
Own income	0-3000 CHF 3001-6000 CHF >6000 CHF	0.85 (0.58-1.24); p=0.396 1.26 (0.87-1.84); p=0.227 Ref.	1.01 (0.56-1.83); p=0.975 1.23 (0.78-1.96); p=0.376 Ref.	0.011
Desired profession	No Partially Yes	2.14 (1.53-2.99); p<0.001[#] 1.43 (1.04-1.97); p=0.026 Ref.	1.84 (1.15-2.94); p=0.011 1.51 (1.02-2.23); p=0.038 Ref.	0.029
Degree of health-related limitations in career choice	Strongly Moderately Not at all	4.42 (2.50-7.83); p<0.001[#] 2.32 (1.59-3.40); p<0.001[#] Ref.	4.79 (2.30-9.96); p<0.001 2.61 (1.64-4.15); p<0.001 Ref.	0.063
Estimation of adequacy of job qualification	Lower Higher Adequate	1.25 (0.89-1.77); p=0.195 1.82 (1.18-2.80); p=0.007[#] Ref.	0.86 (0.55-1.35); p=0.515 1.44 (0.87-2.41); p=0.160 Ref.	0.012
Professional experience	<5 years 5-10 years >10 years	0.48 (0.35-0.66); p<0.001[#] 1.03 (0.75-1.41); p=0.875 Ref.	0.44 (0.28-0.71); p=0.001 1.02 (0.67-1.57); p=0.916 Ref.	0.033
Duration of current employment	<1 year 1-5 years 6-10 years >10 years	0.59 (0.38-0.91); p=0.017 0.82 (0.57-1.17); p=0.268 0.98 (0.65-1.48); p=0.931 Ref.	0.84 (0.47-1.50); p=0.552 1.14 (0.71-1.84); p=0.584 0.99 (0.60-1.65); p=0.975 Ref.	0.011
Work-related stress level	1 point increase [a]	1.09 (1.03-1.15); p=0.002[#]	1.04 (0.97-1.12); p=0.230	0.014

Note

[#] Statistically significant at Bonferroni corrected α=.007

[a] On a scale from 0 (not stress at all) to 10 (extremely severe stress)

[b] Adjusted for all other predictor variables plus nationality, occupation, and number of pregnancies

Results of the main outcome measures “health influences on career choice”, “desired profession” and “professional experience” are highly significant; even if the proportion of variance explained by the last two factors was rather small. Excluding participants who are members of self-help groups did not alter the results.

The intensity of reported health-related limitations in career choice was independent from rASRM-stage ($\chi 2$, 16.51, df=12, p=0.169), but associated with the occurrence of chronic pain ($\chi 2$, 34.39, df=4, p<0.001) as well as with the frequency of pain ($\chi 2$, 25.62, df=8, p=0.001).

Chronic pain was also associated with higher levels of stress at work, even if the mean difference was small (6.61 vs 5.47, SD=2.39/2.49, p<0.001).

Intraoperative findings of spread of endometriosis lesions showed varying associations with health-related limitations in career choice: having endometriosis lesions at the pelvic wall ($\chi 2$, 11.14, df=4, p=0.025) or in the sacrouterine ligaments ($\chi 2$, 13.51, df=4, p=0.009) was significantly associated with greater limitations in career choice, while such an outcome could not be found for localization in the vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50, SD=2.46/2.48, p=0.001), but not with other intraoperative findings.

Work impairment and compensatory mechanisms

Asked about the amount of sick leave due to endometriosis during the last month, 78.1% of the women of the case group reported no sick leave, 8.5% reported one to

three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and 8.1% reported two to four weeks.

Altogether, 13.1% of endometriosis patients used one week or more of overtime or vacation during the last year when they felt too sick to work due to symptoms of endometriosis. Furthermore, 75.5% of women with endometriosis reported to have gone to work during the previous month in spite of severe pain. Asked about the previous year, 89.2% of women with endometriosis affirmed to have worked despite pain. Out of the women diagnosed with endometriosis, 89.8% noted a loss of work productivity due to endometriosis, with 65.1% reporting strong or very strong limitations when symptoms were severe. On days with minimal endometriosis symptoms, 75.3% still felt some degree of loss of productivity.

A minority of women with endometriosis reported working part time (10.3%) or giving up work entirely (5.8%) due to their disease (n=445).

Association of endometriosis-related symptoms with sick leave and productivity loss

We then examined whether different endometriosis symptoms were related to absenteeism and impaired work productivity (Table IV).

Table IV: Association of endometriosis-related symptoms to sick leave and productivity loss in the last month

Predictor		Sick leave [a]		Productivity loss [b]	
		OR (95% CI)	R^2	OR (95% CI)	R^2
Chronic pain	Yes	3.52 (2.02; 6.13); p<0.001[#]	0.072	3.08 (2.11; 4.50); p<0.001[#]	0.087
	No	Ref.		Ref.	
Frequency of pain	Daily	2.82 (1.47; 5.39); p=0.002[#]	0.053	1.81 (1.05; 3.12); p=0.032	0.040
	>1 per week	1.40 (0.66; 2.97); p=0.377		0.76 (0.42; 1.38); p=0.369	
	≤1 per week	Ref.		Ref.	
Frequency of fatigue	Frequently	3.50 (1.76; 6.94); p<0.001[#]	0.073	3.99 (2.49; 6.39); p<0.001[#]	0.107
	Sometimes	1.15 (0.50; 2.64); p=0.748		1.44 (0.86; 2.41); p=0.168	

	Rarely	Ref.		Ref.	
Psychological symptoms [c]	Yes No	3.03 (1.77; 5.18); p<0.001[#] Ref.	0.061	2.90 (1.98; 4.23); p<0.001[#] Ref.	0.082

Note

[#] Statistically significant at Bonferroni corrected α=0.01

[a] Refers to the last 4 weeks; Scale: 1=”never”, 2=1-7 days, 3=>7 days

[b] Refers to current maximal impairments; Scale: 1=”not at all/little”, 2=”moderately/strong”, 3=”very strong”

[c] depressive mood/anxiety/reduced resilience of more than three months

Corrected for multiple testing, all four predictor variables were significantly associated with sick leave during the previous four weeks. The occurrence of chronic pain as well as the frequency of fatigue and concomitant psychological symptoms were associated with significantly higher degrees of perceived productivity loss. Including age and time since diagnosis as potential confounders did not alter the results. Likewise, the factor of different localisations of endometriosis was not associated with sick leave or productivity loss (all p>0.05).

Discussion

Endometriosis is associated with impairment of professional activity: women diagnosed with endometriosis showed a lower likelihood of working in their desired profession and stronger health-related limitations in their career decisions. In contrast, they had professional experience of longer durations. All of these main outcomes were not reported previously and open new insights into the professional life of women with endometriosis. Endometriosis-associated symptoms and symptom characteristics were moderately related to sick leave and loss of productivity, but in

contrast to our expectations, endometriosis was not associated with increased work-related stress levels.

In contrast to remarkable differences regarding parameters of working life, education level did not differ significantly between case and control groups (Table I); this is a result that has been described previously.[13] Other studies, however, reported serious effects of endometriosis on education level, especially on tertiary formation.[8 20] These contrasting findings might result from differences in study groups, e.g. with regard to the onset of disease symptoms in relation to education, professional training and professional activity. Many studies report an average age of first symptoms between 20 and 29 years,[6 31-33]. In our study the average age of diagnosis is 33.7 years. Even if many of these women report the onset of endometriosis-related symptoms several years before diagnosis, it is still an age at which most women have completed professional training. As a consequence, the women investigated in such cohorts will not experience a negative impact of endometriosis on their education, because they were still symptom-free at this age. Other authors reported an earlier onset of disease symptoms,[34] and emphasized that endometriosis in adolescent girls was an underestimated problem.[33 35 36] Consequently, those women, which suffer from endometriosis symptoms already at a young age, might feel limitations due to the disease also early in life, namely already during education.

On the other hand, there might be a higher tolerance for sick leave and impaired energy levels in a school or university setting compared to in paid employment.

Health issues are important criteria in career choice, and women diagnosed with endometriosis do work less often in their desired profession. However, women with endometriosis reported a greater length of experience in the current profession

(Table IIIb). Professional experience and the length of time a woman is working with the current employer are highly correlated. These results can be interpreted positively in the sense that women with endometriosis were successful in carefully choosing a long-term profession. On the other hand, women might feel less able to change the professional field and stuck in an undesired profession because of endometriosis.

Several authors reported elevated levels of general[37 38] as well as emotional[21] distress in women diagnosed with endometriosis. This first study on work-specific stress in endometriosis affected women produced results in contrast to our expectations. Even though women reported that they sometimes went to work despite endometriosis-associated pain, women with endometriosis did not experience higher work-related stress levels than the control women; but within the group of women with endometriosis, those with chronic pain reported significantly higher work-related stress than those without pain. We investigated women whose initial diagnosis was up to 20 years ago; these women may have meanwhile found an occupation meeting their needs, and superiors and colleagues may have adapted to their sometimes reduced availability for work. Also, the fact that work can be a source of distraction and of self-esteem for individuals suffering from a chronic disease[39] may offset stressful situations.

According to our results and those of others,[34] women affected by endometriosis compensate for their health-related restrictions at work by using overtime or vacation for absences as well as by saving energy for work through reduction of leisure time activities.

Despite these personal efforts to adapt to an adverse situation, productivity loss[9 15] and sick leave[9 10] are relevant issues for many women diagnosed with endometriosis. Average loss of work time per week (absenteeism) due to endometriosis is reported to be between 4.4 and 7.4 hours.[9 10] In our study, chronic pain, the frequency of pain, fatigue, and psychological symptoms, such as self-reported depression and anxiety, were significantly - but with modest effect sizes - related to taking more sick leave (Table IV). Productivity loss at work due to endometriosis-related symptoms was described to be high or very high – depending on the current severity of symptoms – by up to 65% of women in the present study. Struggles to fulfil normal demands of work might be exacerbated by the side effects of treatment, for example by dizziness from strong pain killers.[18 19] Although, the majority of women affected with endometriosis seemed to be able to compensate for disease-related difficulties at work and to realize successful long-term professional activity, 16.2% of the women nevertheless reduced or even gave up work entirely due to endometriosis-related symptoms; this is a situation that has been observed also by others.[13] Furthermore, a very similar percentage of women with endometriosis and control women worked part time, even though women diagnosed with endometriosis remained childless more often. Such decisions may result from feeling pressured to reduce or quit work when employers know about a chronic disease such as endometriosis.[8 20] More flexible work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted physical demands, the possibility to lie down, and the existence of bathrooms nearby are seen to be helpful resources for successful professional performance in women with endometriosis.[19 20]

As for the relationship between rASRM stage and endometriosis-associated symptoms,[1 3] none of the parameters evaluating professional activity showed any

significant association with rARSM stage. Testing the association between different intraoperative findings of endometriotic lesions and work outcomes showed inconsistent results. In contrast, most outcome measures were related to the occurrence and frequency of chronic pain; this result is supported by other studies on endometriosis,[10 15] as well as on other chronic pain conditions such as migraine or fibromyalgia.[40 41] Even if the effect size of pain on work in this study is limited, findings support the relevance of pain management for satisfactory work performance. Fatigue, either as a symptom of endometriosis or as a frequent comorbidity,[42] interfered with professional activity in this as well as in other studies.[1 9] In summary, it may be that women with endometriosis strive for normality at their work place, even if it is associated with reduced professional flexibility or with giving up the desire for another profession.

This study presents one of the largest samples investigating the association between endometriosis and professional life and it is one of the very few studies providing a control group. Study participants were recruited in university hospitals, in district hospitals and in doctors' practices in order to collect a representative sample. The pair matching with regard to age and ethnic background reduced the confounding effect of these factors. A meticulous review of all surgical records by the same investigator (AKS) ensured high data quality with regard to diagnosis and classification of endometriosis. The response rate of 64.1% in the case group is in the upper level of comparable studies,[8 9] whereas the response rate of 35.8% in the control group is comparatively low. We cannot exclude that women with a particularly high work load refrained from study participation; however, such an effect is equally relevant in women diagnosed with endometriosis and in controls. The higher

response rate in women with endometriosis supports the fact that such an association does not represent a particular problem for members in this group.

Given the methodology of a self-reported questionnaire answered retrospectively, distortions in the sense of falsely or overly attributing dissatisfaction on the job to endometriosis cannot be excluded. By addressing questions on professional activity either current or in the period just prior to study participation, we tried to reduce recall bias. As we included only patients with a confirmed diagnosis of endometriosis, and as such a confirmation can be provided only by surgery, there may be referral bias. For example, affected but asymptomatic women and symptomatic women who do not have access to or refused surgery might have been excluded. In contrast, asymptomatic women with endometriosis might have been included in the control group which would result in underestimation of results. As we have no differentiated information on symptoms resulting from diseases other than endometriosis, in both groups further confounders might be present; this would also result in underestimation of our findings. A comparison group for the questions of sick leave and productivity loss at work would have been beneficial. However, analysis of impact of different endometriosis-related symptoms on these two outcomes allowed for indirect conclusions on the association between endometriosis and reduced working ability, as well as basic data to design future studies.

Conclusion

Even if most measured effect sizes of associations between endometriosis and individual parameters of working life were small, the study confirms a burdensome influence of the disease on the working life of women affected by endometriosis. Therefore, medical and psychological support should address such issues in order to

support women in adjusting their professional choices and professional development to individual endometriosis-related conditions. Furthermore, for professionals in occupational medicine, insurances, politics etc. it might be useful to know about endometriosis-related challenges and limitations in professional activity.

Acknowledgements

We thank all participating women for supporting our study. We gratefully acknowledge the support of Brigitte Alvera, Valerie Bernays, Theodosia Charpidou, Anna Dietlicher, Franziska Graf, Franka Grischott, Elvira Gross, Nicole Kuenzle, Judith Kurmann, Christina Liebermann, Ilona Lukas, Elena Lupi, Sarah Schaerer, Karoline Stojanov and the self-help groups in data collection. We thank Salome Looser Ott, PhD, and Kathryn Imboden for critical linguistic revision of the manuscript.

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AKS: investigator, collection of data on site in Winterthur, Switzerland, verification of surgical reports, finalization of the manuscript

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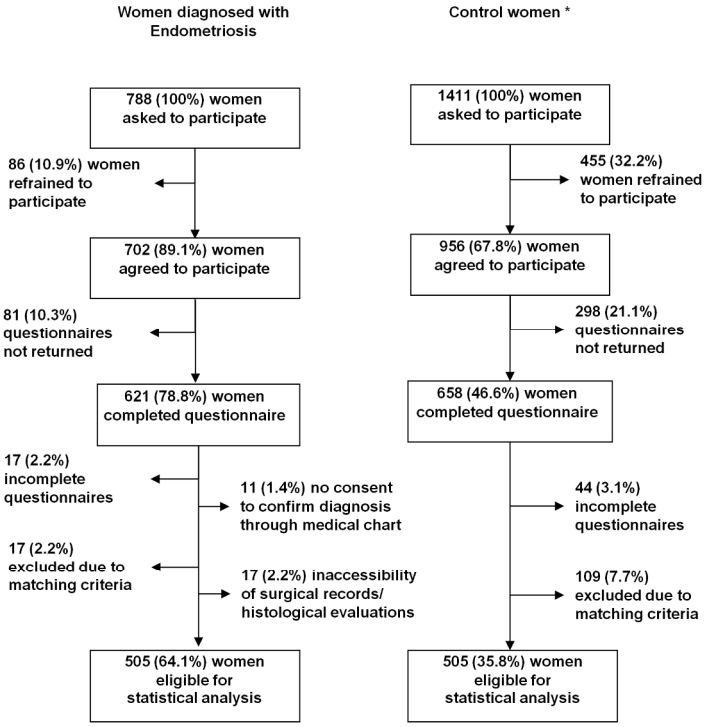
Figure Legend

Fig 1.: Recruitment of study participants

Flow chart I. Recruitment of study participants



* women presenting for routine gynaecological care or benign gynaecological surgery

190x274mm (284 x 284 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8/9*
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Does endometriosis affect professional life? – a matched case-control study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019570.R3
Article Type:	Research
Date Submitted by the Author:	11-Jun-2018
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Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

Does endometriosis affect professional life? – a matched case-control study

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Short title: Endometriosis and professional life

Word count: 4581

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Abstract

Objectives: Endometriosis is a gynaecological disease most commonly causing severe and chronic pelvic pain as well as an impaired quality of life. The aim of this study was to investigate if and how endometriosis affects choices regarding professional life as well as the quality of daily working life.

Design, setting, and participants: In the context of a multicentre case-control study, we collected data from 505 women with surgically/histologically confirmed diagnosis of endometriosis and 505 matched controls. Study participants were recruited prospectively in hospitals and doctors' practices in Switzerland, Germany, and Austria. Using a detailed questionnaire, the study investigated work-life and career choices of study participants.

Main outcome measures: Associations between endometriosis/ disease symptoms and limitations in career development as well as ability to work.

Results: Women with endometriosis were less often able to work in their desired profession than women from the control group (adjusted OR=1.84, 95%-CI: 1.15-2.94, R^2=0.029, p=0.001 and they had to take health-related limitations into consideration in their career decisions to a significantly higher degree than women in the control group (aOR=4.79, 95%-CI: 2.30-9.96, R^2=0.063, p<0.001). Among women with endometriosis, chronic pain was significantly associated with increased sick leave (OR=3.52, 95%-CI: 2.02-6.13, R^2=0.072, p<0.001) as well as with loss of productivity at work (OR=3.08, 95%-CI: 2.11-4.50, R^2=0.087, p<0.001).

Conclusions: Endometriosis is associated with impairment of professional life, in particular with regard to career choices. Further research to develop strategies to

support endometriosis-affected women in realizing professional opportunities is recommended.

Strengths and limitations of this study

This study presents one of the largest samples investigating the association between endometriosis and professional activity. It is one of the first studies in this field to provide a matched control group.

Recruitment of study participants in university hospitals, in district hospitals and in private doctors' practices ensured a representative sample.

Validation of diagnosis and stage of endometriosis by case reports provided high data quality.

Given the design of the study (using a self-reported questionnaire answered retrospectively), distortions in the sense of false or excessive attribution of professional dissatisfaction to endometriosis cannot be excluded.

As we did not investigate diseases or symptoms that may also have had an impact on professional life in the control group, results may be underestimated.

Trial registration number

Clin.trial.gov: Endo_QOL NCT02511626

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors do not have any conflicts of interest.

Data sharing statement

The data set is available on request from the corresponding author.

Key words: Endometriosis, work, professional life, stress, career choice

Introduction

Endometriosis is a gynaecological disease defined by the presence of endometrium-like tissue outside the uterine cavity.[1] The prevalence of the disease among women of reproductive age is estimated to be between 8 and 10%.[2 3] However, as reliable diagnosis of endometriosis can only be made by surgery and endometriosis can be asymptomatic, an unknown number of affected women might remain undiagnosed e.g. prevalence might be far higher.[4]

Women suffering from endometriosis experience most commonly one or more of the following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia, pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea, as well as reduced fertility and chronic fatigue.[5 6 7] Numerous and severe symptoms, the chronicity of the disease[8], side effects of therapies[9] as well as diagnostic delays[10 11] significantly affect women's overall quality of life, including professional performance, and place high demands on the treating physicians.[12 13 14] For most patients, available treatment options, such as analgesics, various hormonal therapies, and radical laparoscopy[1] are often not curative and are associated with significant side effects.[12 15]

Consequently, disease symptoms, especially endometriosis-related pain and fatigue, may disturb the development and realization of long-term goals such as a professional career[16] and may make it difficult to meet the demands of a job. About 40% of women with endometriosis report impaired career growth due to endometriosis,[13] and about 50% experience a decreased ability to work due to their chronic disease.[12 17] Differentiated knowledge on the nature of such limitations and in particular on how adjustments to professional life can be made to improve professional performance is currently lacking.

The quality of working life is a major aspect in quality of life overall,[18] which in turn is the most important predictor of total cost of disease.[19] About 66% to 75% of the total costs of endometriosis arise from reduced ability to work and not from direct costs of treatment.[19 20] Being able to work in a desired occupation may not only have a strong impact on a woman's financial situation and on the perception of and attitude toward daily work, but can also be an important health factor. For example, unsatisfactory work and limited possibilities for change are associated with increased levels of headache, fatigue and depressed mood.[21]

Frequent sick leave and reduced work productivity can put affected women under observation by superiors and under greater pressure to deliver full performance.[22 23] The rather intimate and gender-specific nature of the most common endometriosis symptoms tends to make affected women feel embarrassed.[24] Consequently, some women may avoid discussing endometriosis-related problems with superiors and colleagues, particularly if the superiors and colleagues are male.[24 25] Due to the invisibility of their disease, women can be easily perceived as malingerers.[24] Therefore, medical professionals need to know how the symptoms of endometriosis can affect daily working life and professional development, notably because endometriosis-affected women repeatedly underline their wish for comprehensive

information[24 26 27] and advice in managing their disease in daily life,[26 27] instead of isolated treatment of endometriosis symptoms.[24 26 27] A better understanding of endometriosis and its impacts on any aspect of life - including professional activity - not only by medical professionals but also in society and politics would help affected women and their families to reduce negative consequences of the disease. However, research on quantitative and qualitative impairment of working life as the necessary background for offering adequate support and interventions is scarce and relies mainly on interview-based studies with small samples of affected women[23 24]; there is only one other study that uses a control group.[14] In addition, work-related stress in women diagnosed with endometriosis has not been investigated yet.

Therefore, it was the aim of the present study to investigate parameters of working life of a larger number of endometriosis-affected women, and compare findings with those of a matched control group. We investigated (i) perceived health-related limitations in career decisions; (ii) quality of the current work situation; and (iii) the association between endometriosis-related disease symptoms and work performance.

Material and Methods

Study design

The study is designed as a multicentre case-control study. Main outcome measures are health limitations in career choice as well as quality and stability of the current work situation. Secondary outcome measures investigate the impact of different symptoms as well as localisation of endometriosis on sick leave and loss of

productivity. The study has been conducted and reported applying the criteria of the STROBE Statement.[28]

Recruitment

Recruitment of study participants is shown in Figure I. To detect a 10% difference between cases and controls with an alpha of 0.05, and a power of 0.8 a sample size of 387 participants in each group is needed. With the inclusion of 505 participants in both groups we consequently reached very high power, for example 99.1 for the detection of differences in desired profession or 99.7 for health-related limitations in career choice. Study participants were recruited prospectively for a research project on quality of life including professional activity in endometriosis-affected women compared to control women.[7 9 29 30 31] Recruitment took place between January 2010 and December 2015 at the following hospitals and associated doctors' offices in Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen, Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen, and the University Hospital Graz. In doctors' offices one or several gynecologists work together in a medical unit; district hospitals offer tertiary care associated with a university.

Healthcare professionals carried out the recruitment of all study participants via direct approach. The study was explained to the respondents and information about the voluntary nature of participation as well as anonymity of data in reports and publications was provided. Each participant received a detailed written description of the study and signed informed consent. Participants were given all documents and a return envelope.

Inclusion criteria: All study participants had to be between 18 and 50 years old. For the case group, women with surgically and histologically diagnosed endometriosis were included irrespective of stage, location of lesions, and severity and profile of symptoms. Only data sets with at least 80% of answers for main and secondary outcome measures were included.

Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic, mental or psychological impairments that might affect their ability to understand and to complete the questionnaire.

The most frequent reasons reported for not participating were lack of time and the intimate nature of some of the questions. To maximize the return rate, women were reminded to complete and return the questionnaire after one month and after three months.

A smaller segment of the case group (N=74, 66 of which could be included in the final analysis (13.1% of total case group)) was recruited through different self-help groups for endometriosis patients (in Germany only). Education levels and family incomes in this cohort are similar to those in the main group. However, the women in this cohort were significantly older than those in the hospital group (42.45±6.03 versus 37.02±7.21 years, $p<0.001$), showed a longer time since primary diagnosis (82.11±8.36 versus 37.20±44.00 months, $p<0.001$), and presented at the time of the study a significantly higher stage of disease ($p=0.013$).

Control women were recruited during regular annual or biennial gynaecological consultations at hospitals' out-patient clinics or in private offices, as part of standard healthcare in the three countries where recruitment took place. In addition, women during hospital stays because of temporary mild benign gynaecological problems other than endometriosis were invited to participate in the study. Each control woman

was matched to a woman diagnosed with endometriosis for age (±3 years) and ethnic background, i.e. Caucasian or not (pair matching).

Questionnaire

The structured self-administered questionnaire for the total study on quality of life contained 390 questions for all participants and 90 additional specific questions for women diagnosed with endometriosis. It is structured in different chapters, one of which is professional life. Further chapters covered questions regarding life style; general wellbeing; general, gynaecological, and medical history; childhood experiences; sexuality and partnership. Women diagnosed with endometriosis were additionally asked to provide detailed information on the diagnosis and treatment of endometriosis, symptoms of endometriosis, sick leave, and productivity loss due specifically to endometriosis. Wherever possible we used internationally validated questionnaires. Modified versions of the Brief Pain Inventory[32] and the Pain Disability Index[33 34] served to evaluate pain. For several questions about professional life as for occupation, sick leave and productivity loss, we used similar reporting methods the WPAI[35] suggests, but extended the time period of reporting from only seven days in the WPAI to four weeks and one year. Level of education was measured with defined categories following the recommendation to use meaningful benchmarks of educational attainment rather than a continuous scale in years.[36] In order to capture the professional situation of women diagnosed with endometriosis as close to reality as possible a interdisciplinary research team including specialists for minimally invasive endometriosis-surgery, for gynaecological endocrinology and for gynaeco-psychosomatic medicine added their clinical experience and evaluated systematically what they had learned from individual patients. On this background specific questions like on working despite pain or on using overtime or holidays to compensate for sick

leave were added. The first version of our questions on professional activity was than revised by the governing body of the German self-help groups in order to map the questions to the situations reported by women with endometriosis and to avoid using questions, which do not correctly depict the specific situation in the context of endometriosis.

The analysis presented in this paper was based on answers to the following questions asked to the case as well as to the control group: nationality (German, Swiss, Austrian, other [with the possibility of entering nationality]), age (years), marital status (married/cohabiting/single), highest achieved education level (lower school education, high school education, apprenticeship, university degree, no formal education, other), current own monthly net income (six choices for responses ranging from none to >2500 Euros for participants in Germany and Austria and from none to >6000 Swiss francs for participants in Switzerland), numbers of pregnancies of more than 24 weeks of gestation. Women were asked to report their levels of current employment (full-time/part-time/full-time housekeeping/student/registered as unemployed) and whether they currently worked in their desired profession (yes/no). This question does not ask about the current place of employment but on the profession itself, e.g. for a woman who always wanted to be a teacher, is she now able to work as a teacher? They were asked how they perceived their level of qualification for the currently held job (overqualified, about right, under-qualified), length of professional experience (<5 years, 6-10 years, and >10 years), years working with the current employer (<1 year, 1-5 years, 6-10 years, >10 years), the subjectively perceived influence of health-related limitations on career choice (not at all, little, medium, strongly, exclusively) and perceived current level of stress on the job (scale from 0=none to 10=very strong).

The analysis presented in this paper further used the following questions asked only to women diagnosed with endometriosis: Amount of time since first symptoms of endometriosis were noticed (<1 year ago/1 year ago/2-5 years ago/6-10 years ago/>10 years ago), date of initial diagnosis of endometriosis (month and year), number of surgeries related to endometriosis (1/2/3/4/5/6 or more), chronic pain (yes/no), duration of pain (<1 year/1-3 years/4-5 years/6-10 years/11-20 years/>20 years), frequency of pain (a few times per year/a few times per month/several times per week/once a day/several times a day/permanently), cyclic pain (yes/no), psychological symptoms lasting more than three months estimated by the study participant to be related to endometriosis, such as depressive mood/anxiety/reduced resilience (yes/no), days worked despite pain during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to endometriosis (never/rarely/sometimes/often/very often), sick leave due to symptoms of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/>12 weeks), estimated loss of productivity due to endometriosis when symptoms are at their maximum or at their minimum respectively (no loss/a little/somewhat/high), reduction of work time due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included cyclic as well as non-cyclic pelvic pain.)

The study was registered at clinicaltrials.gov (NCT 02511626), where further details on the complete questionnaire are available.

Verification of diagnosis and stage of endometriosis

To verify diagnosis and obtain information about localization of endometriosis lesions, surgical records as well as the histological diagnosis of each patient and each intervention were collected from medical charts. Stage was classified according to the revised Classification of the American Society for Reproductive Medicine (rASRM).[37]

Ethical approval

The study was approved by the Swiss ethics commission as well as by the ethics boards of participating hospitals. This study followed the guidelines of the World Medical Association Declaration of Helsinki 1964, updated in October 2013.

Patient and Public Involvement statement

Questions for this study were selected in cooperation with endometriosis self-help groups. Other than in the self-help groups patients were not involved in the recruitment and conduct of the study. All interested study participants receive the publications resulting from the study. Publications are also sent to the governing body of the self-help groups.

Statistical analysis

Differences in sample characteristics between study groups were computed with either independent sample t-tests for continuous variables or Pearson $\chi 2$-tests for categorical variables. To test associations between study groups and characteristics of professional life, we conducted a series of binomial logistic regression. The study group, i.e. women with endometriosis as opposed to controls without endometriosis, was included as the dependent variable. To test association between symptoms of endometriosis and work outcomes in women with endometriosis, we conducted a

series of ordinal logistic regression, entering work outcomes as the dependent variable. The proportion of variance explained based on the study group was indicated by Nagelkerke's pseudo R^2. Sample characteristics that differed significantly between study groups were statistically adjusted for by including them simultaneously as covariates. Initially, α was set at 5%, but we applied Bonferroni correction to adjust the significance level α for multiple testing. All analyses were conducted with SPSS version 24 for Windows.

Results

Characteristics of study groups and possible confounders

A comparison of socio-epidemiological parameters between women with endometriosis and control women is presented in Table I. Significant variables, eg nationality, pregnancies, and paid employment, were included as covariates in subsequent analyses on case-control effects.

Table I: Descriptive statistics and group comparisons

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 [a]
Nationality	Swiss German Others	N=211 (42.2%) N=244 (48.8%) N=45 (9.0%)	N=285 (57.3%) N=161 (32.4%) N=51 (10.3%)	p<0.001 [b]
Marital status	Married/ Cohabiting Single	N=420 (83.3%) N=84 (16.7%)	N=397 (79.4%) N=103 (20.6%)	p=0.109 [b]
Pregnancies >24 weeks	0 1 ≥2	N=331 (70.6%) N=83 (17.7%) N=55 (11.7%)	N=245 (50.9%) N=80 (16.6%) N=156 (32.4%)	p<0.001 [b]
Education level[c]	Low Medium High	N=71 (14.4%) N=245 (49.6%) N=178 (36.0%)	N=74 (14.7%) N=249 (49.4%) N=181 (35.9%)	p=0.990 [b]
Paid occupation	Full-time Part-time None	N=248 (49.8%) N=176 (35.3%) N=74 (14.9%)	N=206 (41.8%) N=186 (37.7%) N=101 (20.5%)	p=0.016 [b]

Occupation among mothers[d] only	Full-time Part-time None	N=30 (22.1%) N=68 (50.0%) N=38 (27.9%)	N=57 (23.9%) N=136 (57.1%) N=45 (18.9%)	p=0.120 [b]

Note

[a] Independent samples t-test

[b] Pearson χ^2-test

[c] Scale: Low="no formal education/lower school education", Medium="higher school education/apprenticeship", High="university degree"

[d] women with at least one pregnancy >24 weeks

Disease characteristics of the endometriosis group are shown in Table II.

Table II: Disease characteristics in women diagnosed with endometriosis

Criteria		Endometriosis Group %	N
Time since occurrence of first symptoms (N=474)	<1 year	5.49%	26
	1 year	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	>10 years	42.19%	200
rASRM-stage of endometriosis (N=502)	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
Number of endometriosis-related surgical interventions (N=505)	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information[a]	7.33%	37
	Mean±SD	1.79±1.27	
Douglas obliteration (N=503)	Yes	26.6%	134
	No	73.4%	369
Involvement of sacrouterine ligaments (N=503)	Yes	61.4%	309
	No	38.6%	194
Involvement of Douglas (N=503)	Yes	72.0%	362
	No	28.0%	141
Intra-abdominal adhesions (N=504)	Yes	74.8%	377
	No	25.2%	127
Involvement of pelvic wall (N=503)	Yes	74.8%	377
	No	25.2%	127
Involvement of vaginal fornix or septum rectovaginal (N=503)	Yes	12.7%	64
	No	87.3%	439

Endometrioma (N=502)	Yes	49.0%	246
	No	51.0%	256
Chronic pain (N=500)	Yes	58.40%	292
	No	41.60%	208
Duration of chronic pain	<1 year	3.48%	10
	1-3 years	13.59%	39
	4-5 years	17.07%	49
	6-10 years	23.34%	67
	11-20 years	29.27%	84
	>20 years	13.24%	38
Frequency of pain	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
Frequency of endometriosis-related fatigue/ exhaustion	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Often	28.14%	141
	Very often	22.55%	113
Psychological Symptoms due to endometriosis[b]	Yes	57.24%	261
	No	42.76%	195

Note

[a] question not answered but diagnosis of endometriosis confirmed with at least one surgical record

[b] depressive mood/anxiety/reduced resilience of more than three months

Parameters of working life

Parameters of professional activity in women diagnosed with endometriosis and control women are presented in Table IIIa.

Table IIIa: Parameters of professional activity in the case and the control group

Criteria	Endometriosis group	N	Control group	N
Own net income per month		**480**		**483**
No income	11.25%	54	15.76%	76
<3000 CHF (1000 EUR) [a]	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500 EUR) [a]	49.17%	236	40.37%	195
>6000 CHF (>2500 EUR) [a]	14.79%	71	15.32%	74
Desired profession		**488**		**482**
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
Degree of health-related limitations in		**486**		**466**

career choice				
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
Estimation of adequacy of job qualification		**459**		**453**
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
Professional experience		**487**		**474**
<5 years	18.89%	92	32.70%	155
5-10 years	25.87%	126	21.10%	100
>10 years	55.24%	269	46.20%	219
Duration of current employment		**442**		**439**
<1 year	14.25%	63	20.27%	89
1-5 years	40.72%	180	41.69%	183
6-10 years	22.17%	98	18.91%	83
>10 years	22.85%	101	19.13%	84
Work-related stress level		**460**		**465**
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24
3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66
7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

Note

[a] different income classes in Switzerland and Germany/ Austria

Spearman correlation between professional experience and length of time in the current employment was r=0.490 (p<0.001).

Associations between endometriosis and work outcomes are presented in Table IIIb. In the adjusted analysis, all predictor variables plus nationality, occupation and number of pregnancies were included simultaneously as covariates.

Table IIIb: Associations between endometriosis and parameters of professional life including the proportion of variance explained by the disease

Predictor	Reference category	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[b]	Pseudo R^2
Own income	0-3000 CHF	0.85 (0.58-1.24); p=0.396	1.01 (0.56-1.83); p=0.975	0.011

	3001-6000 CHF >6000 CHF	1.26 (0.87-1.84); p=0.227 Ref.	1.23 (0.78-1.96); p=0.376 Ref.	
Desired profession	No Partially Yes	2.14 (1.53-2.99); p<0.001# 1.43 (1.04-1.97); p=0.026 Ref.	1.84 (1.15-2.94); p=0.011 1.51 (1.02-2.23); p=0.038 Ref.	0.029
Degree of health-related limitations in career choice	Strongly Moderately Not at all	4.42 (2.50-7.83); p<0.001# 2.32 (1.59-3.40); p<0.001# Ref.	4.79 (2.30-9.96); p<0.001 2.61 (1.64-4.15); p<0.001 Ref.	0.063
Estimation of adequacy of job qualification	Lower Higher Adequate	1.25 (0.89-1.77); p=0.195 1.82 (1.18-2.80); p=0.007# Ref.	0.86 (0.55-1.35); p=0.515 1.44 (0.87-2.41); p=0.160 Ref.	0.012
Professional experience	<5 years 5-10 years >10 years	0.48 (0.35-0.66); p<0.001# 1.03 (0.75-1.41); p=0.875 Ref.	0.44 (0.28-0.71); p=0.001 1.02 (0.67-1.57); p=0.916 Ref.	0.033
Duration of current employment	<1 year 1-5 years 6-10 years >10 years	0.59 (0.38-0.91); p=0.017 0.82 (0.57-1.17); p=0.268 0.98 (0.65-1.48); p=0.931 Ref.	0.84 (0.47-1.50); p=0.552 1.14 (0.71-1.84); p=0.584 0.99 (0.60-1.65); p=0.975 Ref.	0.011
Work-related stress level	1 point increase [a]	1.09 (1.03-1.15); p=0.002#	1.04 (0.97-1.12); p=0.230	0.014

Note

Statistically significant at Bonferroni corrected α=.007

[a] On a scale from 0 (not stress at all) to 10 (extremely severe stress)

[b] Adjusted for all other predictor variables plus nationality, occupation, and number of pregnancies

Results of the main outcome measures “health influences on career choice”, “desired profession” and “professional experience” are highly significant; even if the proportion of variance explained by the last two factors was rather small. Excluding participants who are members of self-help groups did not alter the results.

The intensity of reported health-related limitations in career choice was independent from rASRM-stage ($\chi 2$, 16.51, df=12, p=0.169), but associated with the occurrence of chronic pain ($\chi 2$, 34.39, df=4, p<0.001) as well as with the frequency of pain ($\chi 2$, 25.62, df=8, p=0.001).

Chronic pain was also associated with higher levels of stress at work, even if the mean difference was small (6.61 vs 5.47, SD=2.39/2.49, p<0.001).

Intraoperative findings of spread of endometriosis lesions showed varying associations with health-related limitations in career choice: having endometriosis lesions at the pelvic wall ($\chi 2$, 11.14, df=4, p=0.025) or in the sacrouterine ligaments ($\chi 2$, 13.51, df=4, p=0.009) was significantly associated with greater limitations in career choice, while such an outcome could not be found for localization in the vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50, SD=2.46/2.48, p=0.001), but not with other intraoperative findings.

Work impairment and compensatory mechanisms

Asked about the amount of sick leave due to endometriosis during the last month, 78.1% of the women of the case group reported no sick leave, 8.5% reported one to three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and 8.1% reported two to four weeks.

Altogether, 13.1% of endometriosis patients used one week or more of overtime or vacation during the last year when they felt too sick to work due to symptoms of endometriosis. Furthermore, 75.5% of women with endometriosis reported to have gone to work during the previous month in spite of severe pain. Asked about the previous year, 89.2% of women with endometriosis affirmed to have worked despite pain. Out of the women diagnosed with endometriosis, 89.8% noted a loss of work productivity due to endometriosis, with 65.1% reporting strong or very strong limitations when symptoms were severe. On days with minimal endometriosis symptoms, 75.3% still felt some degree of loss of productivity.

A minority of women with endometriosis reported working part time (10.3%) or giving up work entirely (5.8%) due to their disease (n=445).

Association of endometriosis-related symptoms with sick leave and productivity loss

We then examined whether different endometriosis symptoms were related to absenteeism and impaired work productivity (Table IV).

Table IV: Association of endometriosis-related symptoms to sick leave and productivity loss in the last month

Predictor		Sick leave [a]		Productivity loss [b]	
		OR (95% CI)	R^2	OR (95% CI)	R^2
Chronic pain	Yes No	3.52 (2.02; 6.13); p<0.001[#] Ref.	0.072	3.08 (2.11; 4.50); p<0.001[#] Ref.	0.087
Frequency of pain	Daily >1 per week ≤1 per week	2.82 (1.47; 5.39); p=0.002[#] 1.40 (0.66; 2.97); p=0.377 Ref.	0.053	1.81 (1.05; 3.12); p=0.032 0.76 (0.42; 1.38); p=0.369 Ref.	0.040
Frequency of fatigue	Frequently Sometimes Rarely	3.50 (1.76; 6.94); p<0.001[#] 1.15 (0.50; 2.64); p=0.748 Ref.	0.073	3.99 (2.49; 6.39); p<0.001[#] 1.44 (0.86; 2.41); p=0.168 Ref.	0.107
Psychological symptoms [c]	Yes No	3.03 (1.77; 5.18); p<0.001[#] Ref.	0.061	2.90 (1.98; 4.23); p<0.001[#] Ref.	0.082

Note

[#] Statistically significant at Bonferroni corrected α=0.01

[a] Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

[b] Refers to current maximal impairments; Scale: 1="not at all/little", 2="moderately/strong", 3="very strong"

[c] depressive mood/anxiety/reduced resilience of more than three months

Corrected for multiple testing, all four predictor variables were significantly associated with sick leave during the previous four weeks. The occurrence of chronic pain as well as the frequency of fatigue and concomitant psychological symptoms were associated with significantly higher degrees of perceived productivity loss. Including age and time since diagnosis as potential confounders did not alter the results. Likewise, the factor of different localisations of endometriosis was not associated with sick leave or productivity loss (all p>0.05).

Discussion

Endometriosis is associated with impairment of professional activity: women diagnosed with endometriosis showed a lower likelihood of working in their desired profession and stronger health-related limitations in their career decisions. In contrast, they had professional experience of longer durations. All of these main outcomes were not reported previously and open new insights into the professional life of women with endometriosis. Endometriosis-associated symptoms and symptom characteristics were moderately related to sick leave and loss of productivity, but in contrast to our expectations, endometriosis was not associated with increased work-related stress levels.

In contrast to remarkable differences regarding parameters of working life, education level did not differ significantly between case and control groups (Table I); this is a result that has been described previously.[17] Other studies, however, reported serious effects of endometriosis on education level, especially on tertiary formation.[12 24] These contrasting findings might result from differences in study groups, e.g. with regard to the onset of disease symptoms in relation to education, professional training and professional activity. Many studies report an average age of first symptoms between 20 and 29 years,[10 38-40]. In our study the average age of diagnosis is 33.7 years. Even if many of these women report the onset of endometriosis-related symptoms several years before diagnosis, it is still an age at which most women have completed professional training. As a consequence, the women investigated in such cohorts will not experience a negative impact of endometriosis on their education, because they were still symptom-free at this age.

Other authors reported an earlier onset of disease symptoms,[41] and emphasized that endometriosis in adolescent girls was an underestimated problem.[40 42 43] Consequently, those women, which suffer from endometriosis symptoms already at a young age, might feel limitations due to the disease also early in life, namely already during education.

On the other hand, there might be a higher tolerance for sick leave and impaired energy levels in a school or university setting compared to in paid employment.

Health issues are important criteria in career choice, and women diagnosed with endometriosis do work less often in their desired profession. However, women with endometriosis reported a greater length of experience in the current profession (Table IIIb). Professional experience and the length of time a woman is working with the current employer are highly correlated. These results can be interpreted positively in the sense that women with endometriosis were successful in carefully choosing a long-term profession. On the other hand, women might feel less able to change the professional field and stuck in an undesired profession because of endometriosis.

Several authors reported elevated levels of general[44 45] as well as emotional[21] distress in women diagnosed with endometriosis. This first study on work-specific stress in endometriosis affected women produced results in contrast to our expectations. Even though women reported that they sometimes went to work despite endometriosis-associated pain, women with endometriosis did not experience higher work-related stress levels than the control women; but within the group of women with endometriosis, those with chronic pain reported significantly higher work-related stress than those without pain. We investigated women whose

initial diagnosis was up to 20 years ago; these women may have meanwhile found an occupation meeting their needs, and superiors and colleagues may have adapted to their sometimes reduced availability for work. Also, the fact that work can be a source of distraction and of self-esteem for individuals suffering from a chronic disease[46] may offset stressful situations.

According to our results and those of others,[41] women affected by endometriosis compensate for their health-related restrictions at work by using overtime or vacation for absences as well as by saving energy for work through reduction of leisure time activities.

Despite these personal efforts to adapt to an adverse situation, productivity loss[9 15] and sick leave[9 10] are relevant issues for many women diagnosed with endometriosis. Average loss of work time per week (absenteeism) due to endometriosis is reported to be between 4.4 and 7.4 hours.[13 14] In our study, chronic pain, the frequency of pain, fatigue, and psychological symptoms, such as self-reported depression and anxiety, were significantly - but with modest effect sizes - related to taking more sick leave (Table IV). Productivity loss at work due to endometriosis-related symptoms was described to be high or very high – depending on the current severity of symptoms – by up to 65% of women in the present study. Struggles to fulfil normal demands of work might be exacerbated by the side effects of treatment, for example by dizziness from strong pain killers.[22 23] Although, the majority of women affected with endometriosis seemed to be able to compensate for disease-related difficulties at work and to realize successful long-term professional activity, 16.2% of the women nevertheless reduced or even gave up work entirely due to endometriosis-related symptoms; this is a situation that has been observed also by others.[17] Furthermore, a very similar percentage of women with endometriosis and control women worked part

time, even though women diagnosed with endometriosis remained childless more often. Such decisions may result from feeling pressured to reduce or quit work when employers know about a chronic disease such as endometriosis.[12 24] More flexible work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted physical demands, the possibility to lie down, and the existence of bathrooms nearby are seen to be helpful resources for successful professional performance in women with endometriosis.[23 24]

As for the relationship between rASRM stage and endometriosis-associated symptoms,[1 3] none of the parameters evaluating professional activity showed any significant association with rARSM stage. Testing the association between different intraoperative findings of endometriotic lesions and work outcomes showed inconsistent results. In contrast, most outcome measures were related to the occurrence and frequency of chronic pain; this result is supported by other studies on endometriosis,[14 19] as well as on other chronic pain conditions such as migraine or fibromyalgia.[47 48] Even if the effect size of pain on work in this study is limited, findings support the relevance of pain management for satisfactory work performance. Fatigue, either as a symptom of endometriosis or as a frequent comorbidity,[49] interfered with professional activity in this as well as in other studies.[1 13]

In summary, it may be that women with endometriosis strive for normality at their work place, even if it is associated with reduced professional flexibility or with giving up the desire for another profession.

This study presents one of the largest samples investigating the association between endometriosis and professional life and it is one of the very few studies providing a

control group. Study participants were recruited in university hospitals, in district hospitals and in doctors' practices in order to collect a representative sample. The pair matching with regard to age and ethnic background reduced the confounding effect of these factors. A meticulous review of all surgical records by the same investigator (AKS) ensured high data quality with regard to diagnosis and classification of endometriosis. The response rate of 64.1% in the case group is in the upper level of comparable studies,[12 13] whereas the response rate of 35.8% in the control group is comparatively low. We cannot exclude that women with a particularly high work load refrained from study participation; however, such an effect is equally relevant in women diagnosed with endometriosis and in controls. The higher response rate in women with endometriosis supports the fact that such an association does not represent a particular problem for members in this group.

Given the methodology of a self-reported questionnaire answered retrospectively, distortions in the sense of falsely or overly attributing dissatisfaction on the job to endometriosis cannot be excluded. By addressing questions on professional activity either current or in the period just prior to study participation, we tried to reduce recall bias. As we included only patients with a confirmed diagnosis of endometriosis, and as such a confirmation can be provided only by surgery, there may be referral bias. For example, affected but asymptomatic women and symptomatic women who do not have access to or refused surgery might have been excluded, with the first false categorization might result in over- and the second in underestimation of the results. In contrast, asymptomatic women with endometriosis might have been included in the control group which would result in underestimation of results. As we have no differentiated information on symptoms resulting from diseases other than endometriosis, in both groups further confounders might be present; this would also result in underestimation of our findings. Although we recruited women diagnosed

with endometriosis independent from their acute symptomatology e.g. also those presenting for regular controls, recruitment though hospitals might have resulted in selection of women with more severe disease symptoms. A comparison group for the questions of sick leave and productivity loss at work would have been beneficial. However, analysis of impact of different endometriosis-related symptoms on these two outcomes allowed for indirect conclusions on the association between endometriosis and reduced working ability, as well as basic data to design future studies.

Conclusion

Even if most measured effect sizes of associations between endometriosis and individual parameters of working life were small, the study indicates a burdensome influence of the disease on the working life of women affected by endometriosis. Therefore, medical and psychological support should be sensitised towards such issues in order to support women in managing their working life and adjusting their professional choices and professional development to individual endometriosis-related conditions if needed. Furthermore, for professionals in occupational medicine, insurances, politics etc. it might be useful to know about endometriosis-related challenges and possible limitations in professional activity.

Acknowledgements

We thank all participating women for supporting our study. We gratefully acknowledge the support of Brigitte Alvera, Valerie Bernays, Theodosia Charpidou, Anna Dietlicher, Franziska Graf, Franka Grischott, Elvira Gross, Nicole Kuenzle,

Judith Kurmann, Christina Liebermann, Ilona Lukas, Elena Lupi, Sarah Schaerer, Karoline Stojanov and the self-help groups in data collection. We thank Salome Looser Ott, PhD, and Kathryn Imboden for critical linguistic revision of the manuscript.

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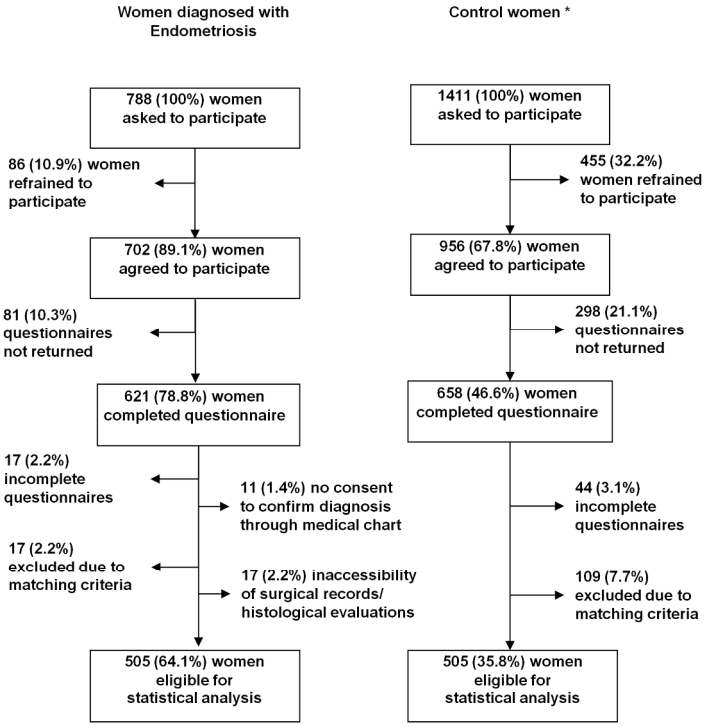
Figure Legend

Fig 1.: Recruitment of study participants

Flow chart I. Recruitment of study participants



* women presenting for routine gynaecological care or benign gynaecological surgery

190x274mm (284 x 284 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8/9*
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Does endometriosis affect professional life? – a matched case-control study in Switzerland, Germany and Austria

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019570.R4
Article Type:	Research
Date Submitted by the Author:	30-Jul-2018
Complete List of Authors:	Sperschneider, Marita; University Hospital Zurich, Department of Reproductive Endocrinology; Canton Hospital Schaffhausen, Department of Gynaecology and Obstetrics Hengartner, Michael; Zurich University of Applied Sciences/ZHAW Kohl-Schwartz, Alexandra; University Hospital Zurich, Department of Reproductive Endocrinology; University Women's Hospital , Division of Gynecological Endocrinology and Reproductive Medicine GEraedts, Kirsten; University Hospital Zurich, Department of Reproductive Endocrinology Rauchfuss, Martina; Charite Berlin, Department of Psychosomatics Woelfler, Monika; Medical University Graz, Department of Gynaecology, Endocrinology and Reproductive Medicine Haeberlin, Felix; Canton Hospital St. Gallen, Department of Gynaecology and Obstetrics von Orelli, Stephanie; Triemli Hospital Zurich, Department of Gynecology and Obstetrics Eberhard, Markus; Canton Hospital Schaffhausen, Department of Gynaecology and Obstetrics Maurer, Franziska; Canton Hospital Solothurn, Department of Gynecology and Obstetrics Imthurn, Bruno; University Hospital Zurich, Department of Reproductive Endocrinology Imesch, Patrick; University Hospital Zurich, Department of Gynaecology Leeners, Brigitte; University Hospital Zurich, Department of Reproductive Endocrinology
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

Does endometriosis affect professional life? – a matched case-control study in Switzerland, Germany and Austria

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Short title: Endometriosis and professional life

Word count: 4581

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Abstract

Objectives: Endometriosis is a gynaecological disease most commonly causing severe and chronic pelvic pain as well as an impaired quality of life. The aim of this study was to investigate if and how endometriosis affects choices regarding professional life as well as the quality of daily working life.

Design, setting, and participants: In the context of a multicentre case-control study, we collected data from 505 women with surgically/histologically confirmed diagnosis of endometriosis and 505 matched controls. Study participants were recruited prospectively in hospitals and doctors' practices in Switzerland, Germany, and Austria. Using a detailed questionnaire, the study investigated work-life and career choices of study participants.

Main outcome measures: Associations between endometriosis/ disease symptoms and limitations in career development as well as ability to work.

Results: Women with endometriosis were less often able to work in their desired profession than women from the control group (adjusted OR=1.84, 95%-CI: 1.15-2.94, R^2=0.029, p=0.001 and they had to take health-related limitations into consideration in their career decisions to a significantly higher degree than women in the control group (aOR=4.79, 95%-CI: 2.30-9.96, R^2=0.063, p<0.001). Among women with endometriosis, chronic pain was significantly associated with increased sick leave (OR=3.52, 95%-CI: 2.02-6.13, R^2=0.072, p<0.001) as well as with loss of productivity at work (OR=3.08, 95%-CI: 2.11-4.50, R^2=0.087, p<0.001).

Conclusions: Endometriosis is associated with impairment of professional life, in particular with regard to career choices. Further research to develop strategies to

support endometriosis-affected women in realizing professional opportunities is recommended.

Strengths and limitations of this study

The study presents one of the largest samples and is one of the first studies providing a matched control group to investigate the association between endometriosis and professional activity.

Recruitment of study participants in university hospitals, in district hospitals and in private doctors' practices ensures a representative sample.

Validation of diagnosis and stage of endometriosis provides high data quality.

The use of a self-reported questionnaire may have caused recall bias.

Due to lack of investigation of diseases or symptoms that may also have influenced professional life in the control group, results may be underestimated.

Trial registration number

Clin.trial.gov: Endo_QOL NCT02511626

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors do not have any competing interests.

Data sharing statement

The data set is available on request from the corresponding author.

Key words: Endometriosis, work, professional life, stress, career choice

Introduction

Endometriosis is a gynaecological disease defined by the presence of endometrium-like tissue outside the uterine cavity.[1] The prevalence of the disease among women of reproductive age is estimated to be between 8 and 10%.[2 3] However, as reliable diagnosis of endometriosis can only be made by surgery and endometriosis can be asymptomatic, an unknown number of affected women might remain undiagnosed e.g. prevalence might be far higher.[4]

Women suffering from endometriosis experience most commonly one or more of the following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia, pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea, as well as reduced fertility and chronic fatigue.[5 6 7] Numerous and severe symptoms, the chronicity of the disease[8], side effects of therapies[9] as well as diagnostic delays[10 11] significantly affect women's overall quality of life, including professional performance, and place high demands on the treating physicians.[12 13 14] For most patients, available treatment options, such as analgesics, various hormonal therapies, and radical laparoscopy[1] are often not curative and are associated with significant side effects.[12 15]

Consequently, disease symptoms, especially endometriosis-related pain and fatigue, may disturb the development and realization of long-term goals such as a professional career[16] and may make it difficult to meet the demands of a job. About 40% of women with endometriosis report impaired career growth due to

endometriosis,[13] and about 50% experience a decreased ability to work due to their chronic disease.[12 17] Differentiated knowledge on the nature of such limitations and in particular on how adjustments to professional life can be made to improve professional performance is currently lacking.

The quality of working life is a major aspect in quality of life overall,[18] which in turn is the most important predictor of total cost of disease.[19] About 66% to 75% of the total costs of endometriosis arise from reduced ability to work and not from direct costs of treatment.[19 20] Being able to work in a desired occupation may not only have a strong impact on a woman's financial situation and on the perception of and attitude toward daily work, but can also be an important health factor. For example, unsatisfactory work and limited possibilities for change are associated with increased levels of headache, fatigue and depressed mood.[21]

Frequent sick leave and reduced work productivity can put affected women under observation by superiors and under greater pressure to deliver full performance.[22 23] The rather intimate and gender-specific nature of the most common endometriosis symptoms tends to make affected women feel embarrassed.[24] Consequently, some women may avoid discussing endometriosis-related problems with superiors and colleagues, particularly if the superiors and colleagues are male.[24 25] Due to the invisibility of their disease, women can be easily perceived as malingerers.[24] Therefore, medical professionals need to know how the symptoms of endometriosis can affect daily working life and professional development, notably because endometriosis-affected women repeatedly underline their wish for comprehensive information[24 26 27] and advice in managing their disease in daily life,[26 27] instead of isolated treatment of endometriosis symptoms.[24 26 27] A better understanding of endometriosis and its impacts on any aspect of life - including professional activity - not only by medical professionals but also in society and politics would help affected

women and their families to reduce negative consequences of the disease. However, research on quantitative and qualitative impairment of working life as the necessary background for offering adequate support and interventions is scarce and relies mainly on interview-based studies with small samples of affected women[23 24]; there is only one other study that uses a control group.[14] In addition, work-related stress in women diagnosed with endometriosis has not been investigated yet.

Therefore, it was the aim of the present study to investigate parameters of working life of a larger number of endometriosis-affected women, and compare findings with those of a matched control group. We investigated (i) perceived health-related limitations in career decisions; (ii) quality of the current work situation; and (iii) the association between endometriosis-related disease symptoms and work performance.

Material and Methods

Study design

The study is designed as a multicentre case-control study. Main outcome measures are health limitations in career choice as well as quality and stability of the current work situation. Secondary outcome measures investigate the impact of different symptoms as well as localisation of endometriosis on sick leave and loss of productivity. The study has been conducted and reported applying the criteria of the STROBE Statement.[28]

Recruitment

Recruitment of study participants is shown in Figure I. To detect a 10% difference between cases and controls with an alpha of 0.05, and a power of 0.8 a sample size of 387 participants in each group is needed. With the inclusion of 505 participants in both groups we consequently reached very high power, for example 99.1 for the detection of differences in desired profession or 99.7 for health-related limitations in career choice. Study participants were recruited prospectively for a research project on quality of life including professional activity in endometriosis-affected women compared to control women.[7 9 29 30 31] Recruitment took place between January 2010 and December 2015 at the following hospitals and associated doctors' offices in Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen, Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen, and the University Hospital Graz. In doctors' offices one or several gynecologists work together in a medical unit; district hospitals offer tertiary care associated with a university.

Healthcare professionals carried out the recruitment of all study participants via direct approach. The study was explained to the respondents and information about the voluntary nature of participation as well as anonymity of data in reports and publications was provided. Each participant received a detailed written description of the study and signed informed consent. Participants were given all documents and a return envelope.

Inclusion criteria: All study participants had to be between 18 and 50 years old. For the case group, women with surgically and histologically diagnosed endometriosis were included irrespective of stage, location of lesions, and severity and profile of symptoms. Only data sets with at least 80% of answers for main and secondary

outcome measures were included.

Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic, mental or psychological impairments that might affect their ability to understand and to complete the questionnaire.

The most frequent reasons reported for not participating were lack of time and the intimate nature of some of the questions. To maximize the return rate, women were reminded to complete and return the questionnaire after one month and after three months.

A smaller segment of the case group (N=74, 66 of which could be included in the final analysis (13.1% of total case group)) was recruited through different self-help groups for endometriosis patients (in Germany only). Education levels and family incomes in this cohort are similar to those in the main group. However, the women in this cohort were significantly older than those in the hospital group (42.45±6.03 versus 37.02±7.21 years, $p<0.001$), showed a longer time since primary diagnosis (82.11±8.36 versus 37.20±44.00 months, $p<0.001$), and presented at the time of the study a significantly higher stage of disease ($p=0.013$).

Control women were recruited during regular annual or biennial gynaecological consultations at hospitals' out-patient clinics or in private offices, as part of standard healthcare in the three countries where recruitment took place. In addition, women during hospital stays because of temporary mild benign gynaecological problems other than endometriosis were invited to participate in the study. Each control woman was matched to a woman diagnosed with endometriosis for age (±3 years) and ethnic background, i.e. Caucasian or not (pair matching).

Questionnaire

The structured self-administered questionnaire for the total study on quality of life contained 390 questions for all participants and 90 additional specific questions for women diagnosed with endometriosis. It is structured in different chapters, one of which is professional life. Further chapters covered questions regarding life style; general wellbeing; general, gynaecological, and medical history; childhood experiences; sexuality and partnership. Women diagnosed with endometriosis were additionally asked to provide detailed information on the diagnosis and treatment of endometriosis, symptoms of endometriosis, sick leave, and productivity loss due specifically to endometriosis. Wherever possible we used internationally validated questionnaires. Modified versions of the Brief Pain Inventory[32] and the Pain Disability Index[33 34] served to evaluate pain. For several questions about professional life as for occupation, sick leave and productivity loss, we used similar reporting methods the WPAI[35] suggests, but extended the time period of reporting from only seven days in the WPAI to four weeks and one year. Level of education was measured with defined categories following the recommendation to use meaningful benchmarks of educational attainment rather than a continuous scale in years.[36] In order to capture the professional situation of women diagnosed with endometriosis as close to reality as possible a interdisciplinary research team including specialists for minimally invasive endometriosis-surgery, for gynaecological endocrinology and for gynaeco-psychosomatic medicine added their clinical experience and evaluated systematically what they had learned from individual patients. On this background specific questions like on working despite pain or on using overtime or holidays to compensate for sick leave were added. The first version of our questions on professional activity was than revised by the governing body of the German self-help groups in order to map the questions to the situations reported by women with endometriosis and to avoid using

questions, which do not correctly depict the specific situation in the context of endometriosis.

The analysis presented in this paper was based on answers to the following questions asked to the case as well as to the control group: nationality (German, Swiss, Austrian, other [with the possibility of entering nationality]), age (years), marital status (married/cohabiting/single), highest achieved education level (lower school education, high school education, apprenticeship, university degree, no formal education, other), current own monthly net income (six choices for responses ranging from none to >2500 Euros for participants in Germany and Austria and from none to >6000 Swiss francs for participants in Switzerland), numbers of pregnancies of more than 24 weeks of gestation. Women were asked to report their levels of current employment (full-time/part-time/full-time housekeeping/student/registered as unemployed) and whether they currently worked in their desired profession (yes/no). This question does not ask about the current place of employment but on the profession itself, e.g. for a woman who always wanted to be a teacher, is she now able to work as a teacher? They were asked how they perceived their level of qualification for the currently held job (overqualified, about right, under-qualified), length of professional experience (<5 years, 6-10 years, and >10 years), years working with the current employer (<1 year, 1-5 years, 6-10 years, >10 years), the subjectively perceived influence of health-related limitations on career choice (not at all, little, medium, strongly, exclusively) and perceived current level of stress on the job (scale from 0=none to 10=very strong).

The analysis presented in this paper further used the following questions asked only to women diagnosed with endometriosis: Amount of time since first symptoms of endometriosis were noticed (<1 year ago/1 year ago/2-5 years ago/6-10 years ago/>10 years ago), date of initial diagnosis of endometriosis (month and year),

number of surgeries related to endometriosis (1/2/3/4/5/6 or more), chronic pain (yes/no), duration of pain (<1 year/1-3 years/4-5 years/6-10 years/11-20 years/>20 years), frequency of pain (a few times per year/a few times per month/several times per week/once a day/several times a day/permanently), cyclic pain (yes/no), psychological symptoms lasting more than three months estimated by the study participant to be related to endometriosis, such as depressive mood/anxiety/reduced resilience (yes/no), days worked despite pain during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to endometriosis (never/rarely/sometimes/often/very often), sick leave due to symptoms of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/>12 weeks), estimated loss of productivity due to endometriosis when symptoms are at their maximum or at their minimum respectively (no loss/a little/somewhat/high), reduction of work time due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included cyclic as well as non-cyclic pelvic pain.)

The study was registered at clinicaltrials.gov (NCT 02511626), where further details on the complete questionnaire are available.

Verification of diagnosis and stage of endometriosis

To verify diagnosis and obtain information about localization of endometriosis lesions, surgical records as well as the histological diagnosis of each patient and each intervention were collected from medical charts. Stage was classified according to the revised Classification of the American Society for Reproductive Medicine (rASRM).[37]

Ethical approval

The study was approved by the Swiss ethics commission as well as by the ethics boards of participating hospitals. This study followed the guidelines of the World Medical Association Declaration of Helsinki 1964, updated in October 2013.

Patient and Public Involvement statement

Questions for this study were selected in cooperation with endometriosis self-help groups. Other than in the self-help groups patients were not involved in the recruitment and conduct of the study. All interested study participants receive the publications resulting from the study. Publications are also sent to the governing body of the self-help groups.

Statistical analysis

Differences in sample characteristics between study groups were computed with either independent sample t-tests for continuous variables or Pearson χ2-tests for categorical variables. To test associations between study groups and characteristics of professional life, we conducted a series of binomial logistic regression. The study group, i.e. women with endometriosis as opposed to controls without endometriosis, was included as the dependent variable. To test association between symptoms of endometriosis and work outcomes in women with endometriosis, we conducted a series of ordinal logistic regression, entering work outcomes as the dependent variable. The proportion of variance explained based on the study group was indicated by Nagelkerke's pseudo R^2. Sample characteristics that differed significantly between study groups were statistically adjusted for by including them simultaneously as covariates. Initially, α was set at 5%, but we applied Bonferroni

correction to adjust the significance level α for multiple testing. All analyses were conducted with SPSS version 24 for Windows.

Results

Characteristics of study groups and possible confounders

A comparison of socio-epidemiological parameters between women with endometriosis and control women is presented in Table I. Significant variables, eg nationality, pregnancies, and paid employment, were included as covariates in subsequent analyses on case-control effects.

Table I: Descriptive statistics and group comparisons

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 [a]
Nationality	Swiss German Others	N=211 (42.2%) N=244 (48.8%) N=45 (9.0%)	N=285 (57.3%) N=161 (32.4%) N=51 (10.3%)	p<0.001 [b]
Marital status	Married/ Cohabiting Single	N=420 (83.3%) N=84 (16.7%)	N=397 (79.4%) N=103 (20.6%)	p=0.109 [b]
Pregnancies >24 weeks	0 1 ≥2	N=331 (70.6%) N=83 (17.7%) N=55 (11.7%)	N=245 (50.9%) N=80 (16.6%) N=156 (32.4%)	p<0.001 [b]
Education level[c]	Low Medium High	N=71 (14.4%) N=245 (49.6%) N=178 (36.0%)	N=74 (14.7%) N=249 (49.4%) N=181 (35.9%)	p=0.990 [b]
Paid occupation	Full-time Part-time None	N=248 (49.8%) N=176 (35.3%) N=74 (14.9%)	N=206 (41.8%) N=186 (37.7%) N=101 (20.5%)	p=0.016 [b]
Occupation among mothers[d] only	Full-time Part-time None	N=30 (22.1%) N=68 (50.0%) N=38 (27.9%)	N=57 (23.9%) N=136 (57.1%) N=45 (18.9%)	p=0.120 [b]

Note

[a] Independent samples t-test

[b] Pearson χ^2-test

[c] Scale: Low="no formal education/lower school education", Medium="higher school education/apprenticeship", High="university degree"

[d] women with at least one pregnancy >24 weeks

Disease characteristics of the endometriosis group are shown in Table II.

Table II: Disease characteristics in women diagnosed with endometriosis

Criteria		Endometriosis Group %	N
Time since occurrence of first symptoms (N=474)	<1 year	5.49%	26
	1 year	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	>10 years	42.19%	200
rASRM-stage of endometriosis (N=502)	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
Number of endometriosis-related surgical interventions (N=505)	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information[a]	7.33%	37
	Mean±SD	1.79±1.27	
Douglas obliteration (N=503)	Yes	26.6%	134
	No	73.4%	369
Involvement of sacrouterine ligaments (N=503)	Yes	61.4%	309
	No	38.6%	194
Involvement of Douglas (N=503)	Yes	72.0%	362
	No	28.0%	141
Intra-abdominal adhesions (N=504)	Yes	74.8%	377
	No	25.2%	127
Involvement of pelvic wall (N=503)	Yes	74.8%	377
	No	25.2%	127
Involvement of vaginal fornix or septum rectovaginal (N=503)	Yes	12.7%	64
	No	87.3%	439
Endometrioma (N=502)	Yes	49.0%	246
	No	51.0%	256
Chronic pain (N=500)	Yes	58.40%	292
	No	41.60%	208
Duration of chronic pain	<1 year	3.48%	10
	1-3 years	13.59%	39
	4-5 years	17.07%	49
	6-10 years	23.34%	67
	11-20 years	29.27%	84
	>20 years	13.24%	38

Frequency of pain	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
Frequency of endometriosis-related fatigue/ exhaustion	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Often	28.14%	141
	Very often	22.55%	113
Psychological Symptoms due to endometriosis[b]	Yes	57.24%	261
	No	42.76%	195

Note

[a] question not answered but diagnosis of endometriosis confirmed with at least one surgical record

[b]depressive mood/anxiety/reduced resilience of more than three months

Parameters of working life

Parameters of professional activity in women diagnosed with endometriosis and control women are presented in Table IIIa.

Table IIIa: Parameters of professional activity in the case and the control group

Criteria	Endometriosis group	N	Control group	N
Own net income per month		**480**		**483**
No income	11.25%	54	15.76%	76
<3000 CHF (1000 EUR)[a]	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500 EUR)[a]	49.17%	236	40.37%	195
>6000 CHF (>2500 EUR)[a]	14.79%	71	15.32%	74
Desired profession		**488**		**482**
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
Degree of health-related limitations in career choice		**486**		**466**
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
Estimation of adequacy of job qualification		**459**		**453**
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
Professional experience		**487**		**474**

<5 years	18.89%	92	32.70%	155
5-10 years	25.87%	126	21.10%	100
>10 years	55.24%	269	46.20%	219
Duration of current employment		**442**		**439**
<1 year	14.25%	63	20.27%	89
1-5 years	40.72%	180	41.69%	183
6-10 years	22.17%	98	18.91%	83
>10 years	22.85%	101	19.13%	84
Work-related stress level		**460**		**465**
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24
3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66
7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

Note

[a] different income classes in Switzerland and Germany/ Austria

Spearman correlation between professional experience and length of time in the current employment was r=0.490 (p<0.001).

Associations between endometriosis and work outcomes are presented in Table IIIb. In the adjusted analysis, all predictor variables plus nationality, occupation and number of pregnancies were included simultaneously as covariates.

Table IIIb: Associations between endometriosis and parameters of professional life including the proportion of variance explained by the disease

Predictor	Reference category	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[b]	Pseudo R^2
Own income	0-3000 CHF 3001-6000 CHF >6000 CHF	0.85 (0.58-1.24); p=0.396 1.26 (0.87-1.84); p=0.227 Ref.	1.01 (0.56-1.83); p=0.975 1.23 (0.78-1.96); p=0.376 Ref.	0.011
Desired profession	No Partially Yes	2.14 (1.53-2.99); p<0.001[#] 1.43 (1.04-1.97); p=0.026 Ref.	1.84 (1.15-2.94); p=0.011 1.51 (1.02-2.23); p=0.038 Ref.	0.029
Degree of health-related limitations in career choice	Strongly Moderately Not at all	4.42 (2.50-7.83); p<0.001[#] 2.32 (1.59-3.40); p<0.001[#] Ref.	4.79 (2.30-9.96); p<0.001 2.61 (1.64-4.15); p<0.001 Ref.	0.063
Estimation of adequacy of job qualification	Lower Higher Adequate	1.25 (0.89-1.77); p=0.195 1.82 (1.18-2.80); p=0.007[#] Ref.	0.86 (0.55-1.35); p=0.515 1.44 (0.87-2.41); p=0.160 Ref.	0.012
Professional	<5 years	0.48 (0.35-0.66); p<0.001[#]	0.44 (0.28-0.71); p=0.001	0.033

experience	5-10 years >10 years	1.03 (0.75-1.41); p=0.875 Ref.	1.02 (0.67-1.57); p=0.916 Ref.	
Duration of current employment	<1 year 1-5 years 6-10 years >10 years	0.59 (0.38-0.91); p=0.017 0.82 (0.57-1.17); p=0.268 0.98 (0.65-1.48); p=0.931 Ref.	0.84 (0.47-1.50); p=0.552 1.14 (0.71-1.84); p=0.584 0.99 (0.60-1.65); p=0.975 Ref.	0.011
Work-related stress level	1 point increase [a]	1.09 (1.03-1.15); p=0.002[#]	1.04 (0.97-1.12); p=0.230	0.014

Note

[#] Statistically significant at Bonferroni corrected α=.007

[a] On a scale from 0 (not stress at all) to 10 (extremely severe stress)

[b] Adjusted for all other predictor variables plus nationality, occupation, and number of pregnancies

Results of the main outcome measures “health influences on career choice”, “desired profession” and “professional experience” are highly significant; even if the proportion of variance explained by the last two factors was rather small. Excluding participants who are members of self-help groups did not alter the results.

The intensity of reported health-related limitations in career choice was independent from rASRM-stage (χ2, 16.51, df=12, p=0.169), but associated with the occurrence of chronic pain (χ2, 34.39, df=4, p<0.001) as well as with the frequency of pain (χ2, 25.62, df=8, p=0.001).

Chronic pain was also associated with higher levels of stress at work, even if the mean difference was small (6.61 vs 5.47, SD=2.39/2.49, p<0.001).

Intraoperative findings of spread of endometriosis lesions showed varying associations with health-related limitations in career choice: having endometriosis lesions at the pelvic wall (χ2, 11.14, df=4, p=0.025) or in the sacrouterine ligaments (χ2, 13.51, df=4, p=0.009) was significantly associated with greater limitations in career choice, while such an outcome could not be found for localization in the vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress

at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50, SD=2.46/2.48, p=0.001), but not with other intraoperative findings.

Work impairment and compensatory mechanisms

Asked about the amount of sick leave due to endometriosis during the last month, 78.1% of the women of the case group reported no sick leave, 8.5% reported one to three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and 8.1% reported two to four weeks.

Altogether, 13.1% of endometriosis patients used one week or more of overtime or vacation during the last year when they felt too sick to work due to symptoms of endometriosis. Furthermore, 75.5% of women with endometriosis reported to have gone to work during the previous month in spite of severe pain. Asked about the previous year, 89.2% of women with endometriosis affirmed to have worked despite pain. Out of the women diagnosed with endometriosis, 89.8% noted a loss of work productivity due to endometriosis, with 65.1% reporting strong or very strong limitations when symptoms were severe. On days with minimal endometriosis symptoms, 75.3% still felt some degree of loss of productivity.

A minority of women with endometriosis reported working part time (10.3%) or giving up work entirely (5.8%) due to their disease (n=445).

Association of endometriosis-related symptoms with sick leave and productivity loss

We then examined whether different endometriosis symptoms were related to absenteeism and impaired work productivity (Table IV).

Table IV: Association of endometriosis-related symptoms to sick leave and productivity loss in the last month

Predictor		Sick leave [a]		Productivity loss [b]	
		OR (95% CI)	R^2	OR (95% CI)	R^2
Chronic pain	Yes No	3.52 (2.02; 6.13); p<0.001[#] Ref.	0.072	3.08 (2.11; 4.50); p<0.001[#] Ref.	0.087
Frequency of pain	Daily >1 per week ≤1 per week	2.82 (1.47; 5.39); p=0.002[#] 1.40 (0.66; 2.97); p=0.377 Ref.	0.053	1.81 (1.05; 3.12); p=0.032 0.76 (0.42; 1.38); p=0.369 Ref.	0.040
Frequency of fatigue	Frequently Sometimes Rarely	3.50 (1.76; 6.94); p<0.001[#] 1.15 (0.50; 2.64); p=0.748 Ref.	0.073	3.99 (2.49; 6.39); p<0.001[#] 1.44 (0.86; 2.41); p=0.168 Ref.	0.107
Psychological symptoms [c]	Yes No	3.03 (1.77; 5.18); p<0.001[#] Ref.	0.061	2.90 (1.98; 4.23); p<0.001[#] Ref.	0.082

Note

[#] Statistically significant at Bonferroni corrected α=0.01

[a] Refers to the last 4 weeks; Scale: 1=”never”, 2=1-7 days, 3=>7 days

[b] Refers to current maximal impairments; Scale: 1=”not at all/little”, 2=”moderately/strong”, 3=”very strong”

[c] depressive mood/anxiety/reduced resilience of more than three months

Corrected for multiple testing, all four predictor variables were significantly associated with sick leave during the previous four weeks. The occurrence of chronic pain as well as the frequency of fatigue and concomitant psychological symptoms were associated with significantly higher degrees of perceived productivity loss. Including age and time since diagnosis as potential confounders did not alter the results. Likewise, the factor of different localisations of endometriosis was not associated with sick leave or productivity loss (all p>0.05).

Discussion

Endometriosis is associated with impairment of professional activity: women diagnosed with endometriosis showed a lower likelihood of working in their desired

profession and stronger health-related limitations in their career decisions. In contrast, they had professional experience of longer durations. All of these main outcomes were not reported previously and open new insights into the professional life of women with endometriosis. Endometriosis-associated symptoms and symptom characteristics were moderately related to sick leave and loss of productivity, but in contrast to our expectations, endometriosis was not associated with increased work-related stress levels.

In contrast to remarkable differences regarding parameters of working life, education level did not differ significantly between case and control groups (Table I); this is a result that has been described previously.[17] Other studies, however, reported serious effects of endometriosis on education level, especially on tertiary formation.[12 24] These contrasting findings might result from differences in study groups, e.g. with regard to the onset of disease symptoms in relation to education, professional training and professional activity. Many studies report an average age of first symptoms between 20 and 29 years,[10 38-40]. In our study the average age of diagnosis is 33.7 years. Even if many of these women report the onset of endometriosis-related symptoms several years before diagnosis, it is still an age at which most women have completed professional training. As a consequence, the women investigated in such cohorts will not experience a negative impact of endometriosis on their education, because they were still symptom-free at this age. Other authors reported an earlier onset of disease symptoms,[41] and emphasized that endometriosis in adolescent girls was an underestimated problem.[40 42 43] Consequently, those women, which suffer from endometriosis symptoms already at a young age, might feel limitations due to the disease also early in life, namely already during education.

On the other hand, there might be a higher tolerance for sick leave and impaired energy levels in a school or university setting compared to in paid employment.

Health issues are important criteria in career choice, and women diagnosed with endometriosis do work less often in their desired profession. However, women with endometriosis reported a greater length of experience in the current profession (Table IIIb). Professional experience and the length of time a woman is working with the current employer are highly correlated. These results can be interpreted positively in the sense that women with endometriosis were successful in carefully choosing a long-term profession. On the other hand, women might feel less able to change the professional field and stuck in an undesired profession because of endometriosis.

Several authors reported elevated levels of general[44 45] as well as emotional[21] distress in women diagnosed with endometriosis. This first study on work-specific stress in endometriosis affected women produced results in contrast to our expectations. Even though women reported that they sometimes went to work despite endometriosis-associated pain, women with endometriosis did not experience higher work-related stress levels than the control women; but within the group of women with endometriosis, those with chronic pain reported significantly higher work-related stress than those without pain. We investigated women whose initial diagnosis was up to 20 years ago; these women may have meanwhile found an occupation meeting their needs, and superiors and colleagues may have adapted to their sometimes reduced availability for work. Also, the fact that work can be a source of distraction and of self-esteem for individuals suffering from a chronic disease[46] may offset stressful situations.

According to our results and those of others,[41] women affected by endometriosis compensate for their health-related restrictions at work by using overtime or vacation for absences as well as by saving energy for work through reduction of leisure time activities.

Despite these personal efforts to adapt to an adverse situation, productivity loss[9 15] and sick leave[9 10] are relevant issues for many women diagnosed with endometriosis. Average loss of work time per week (absenteeism) due to endometriosis is reported to be between 4.4 and 7.4 hours.[13 14] In our study, chronic pain, the frequency of pain, fatigue, and psychological symptoms, such as self-reported depression and anxiety, were significantly - but with modest effect sizes - related to taking more sick leave (Table IV). Productivity loss at work due to endometriosis-related symptoms was described to be high or very high – depending on the current severity of symptoms – by up to 65% of women in the present study. Struggles to fulfil normal demands of work might be exacerbated by the side effects of treatment, for example by dizziness from strong pain killers.[22 23] Although, the majority of women affected with endometriosis seemed to be able to compensate for disease-related difficulties at work and to realize successful long-term professional activity, 16.2% of the women nevertheless reduced or even gave up work entirely due to endometriosis-related symptoms; this is a situation that has been observed also by others.[17] Furthermore, a very similar percentage of women with endometriosis and control women worked part time, even though women diagnosed with endometriosis remained childless more often. Such decisions may result from feeling pressured to reduce or quit work when employers know about a chronic disease such as endometriosis.[12 24] More flexible work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted physical demands, the possibility to lie down, and the existence of bathrooms nearby

are seen to be helpful resources for successful professional performance in women with endometriosis.[23 24]

As for the relationship between rASRM stage and endometriosis-associated symptoms,[1 3] none of the parameters evaluating professional activity showed any significant association with rARSM stage. Testing the association between different intraoperative findings of endometriotic lesions and work outcomes showed inconsistent results. In contrast, most outcome measures were related to the occurrence and frequency of chronic pain; this result is supported by other studies on endometriosis,[14 19] as well as on other chronic pain conditions such as migraine or fibromyalgia.[47 48] Even if the effect size of pain on work in this study is limited, findings support the relevance of pain management for satisfactory work performance. Fatigue, either as a symptom of endometriosis or as a frequent comorbidity,[49] interfered with professional activity in this as well as in other studies.[1 13]

In summary, it may be that women with endometriosis strive for normality at their work place, even if it is associated with reduced professional flexibility or with giving up the desire for another profession.

This study presents one of the largest samples investigating the association between endometriosis and professional life and it is one of the very few studies providing a control group. Study participants were recruited in university hospitals, in district hospitals and in doctors' practices in order to collect a representative sample. The pair matching with regard to age and ethnic background reduced the confounding effect of these factors. A meticulous review of all surgical records by the same investigator (AKS) ensured high data quality with regard to diagnosis and

classification of endometriosis. The response rate of 64.1% in the case group is in the upper level of comparable studies,[12 13] whereas the response rate of 35.8% in the control group is comparatively low. We cannot exclude that women with a particularly high work load refrained from study participation; however, such an effect is equally relevant in women diagnosed with endometriosis and in controls. The higher response rate in women with endometriosis supports the fact that such an association does not represent a particular problem for members in this group.

Given the methodology of a self-reported questionnaire answered retrospectively, distortions in the sense of falsely or overly attributing dissatisfaction on the job to endometriosis cannot be excluded. By addressing questions on professional activity either current or in the period just prior to study participation, we tried to reduce recall bias. As we included only patients with a confirmed diagnosis of endometriosis, and as such a confirmation can be provided only by surgery, there may be referral bias. For example, affected but asymptomatic women and symptomatic women who do not have access to or refused surgery might have been excluded, with the first false categorization might result in over- and the second in underestimation of the results. In contrast, asymptomatic women with endometriosis might have been included in the control group which would result in underestimation of results. As we have no differentiated information on symptoms resulting from diseases other than endometriosis, in both groups further confounders might be present; this would also result in underestimation of our findings. Although we recruited women diagnosed with endometriosis independent from their acute symptomatology e.g. also those presenting for regular controls, recruitment though hospitals might have resulted in selection of women with more severe disease symptoms. A comparison group for the questions of sick leave and productivity loss at work would have been beneficial. However, analysis of impact of different endometriosis-related symptoms on these

two outcomes allowed for indirect conclusions on the association between endometriosis and reduced working ability, as well as basic data to design future studies.

Conclusion

Even if most measured effect sizes of associations between endometriosis and individual parameters of working life were small, the study indicates a burdensome influence of the disease on the working life of women affected by endometriosis. Therefore, medical and psychological support should be sensitised towards such issues in order to support women in managing their working life and adjusting their professional choices and professional development to individual endometriosis-related conditions if needed. Furthermore, for professionals in occupational medicine, insurances, politics etc. it might be useful to know about endometriosis-related challenges and possible limitations in professional activity.

Acknowledgements

We thank all participating women for supporting our study. We gratefully acknowledge the support of Brigitte Alvera, Valerie Bernays, Theodosia Charpidou, Anna Dietlicher, Franziska Graf, Franka Grischott, Elvira Gross, Nicole Kuenzle, Judith Kurmann, Christina Liebermann, Ilona Lukas, Elena Lupi, Sarah Schaerer, Karoline Stojanov and the self-help groups in data collection. We thank Salome Looser Ott, PhD, and Kathryn Imboden for critical linguistic revision of the manuscript.

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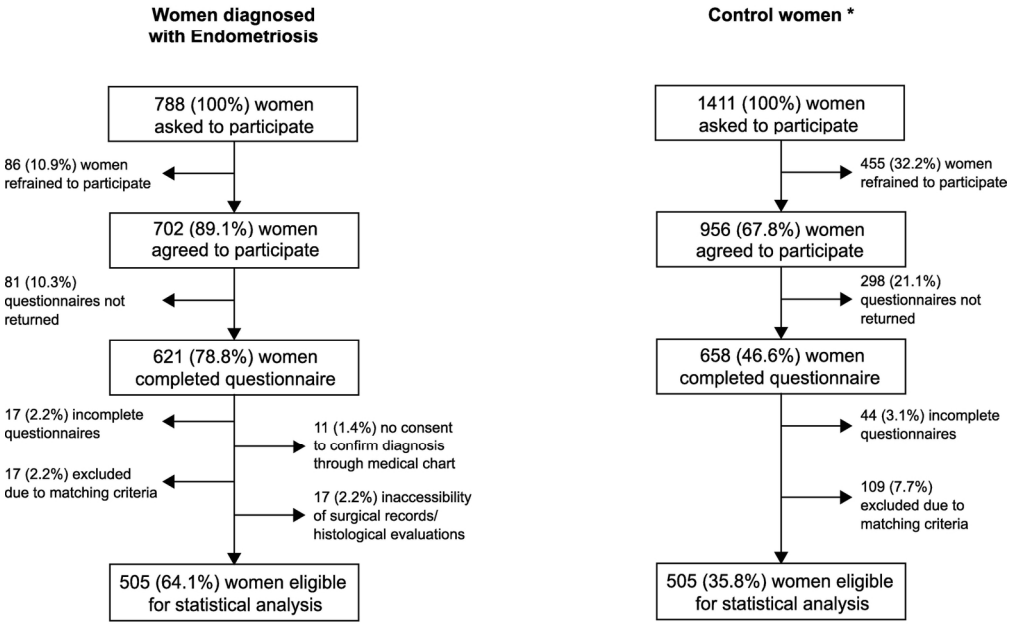
Figure Legend

Fig 1.: Recruitment of study participants

Figure I. Recruitment of study participants



* women presenting for routine gynaecological care or benign gynaecological surgery

157x130mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8/9*
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.